



# **STIC Search Report**

## **Biotech-Chem Library**

**STIC Database Tracking Number: 201638**

**TO: Margaret Seaman**  
**Location: rem/4C89/4C70**  
**Art Unit: 1625**  
**Tuesday, September 19, 2006**  
**Case Serial Number: 10/606027**

**From: John DiNatale**  
**Location: Biotech-Chem Library**  
**REM-1B65**  
**Phone: (571)272-2557**

**john.dinatale@uspto.gov**

### **Search Notes**

Examiner Seaman,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

John DiNatale  
Technical Information Specialist  
STIC Biotech/Chem Library  
(571)272-2557

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

#### FILE CAPLUS

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FILE COVERS 1907 - 19 Sep 2006 VOL 145 ISS 13

FILE LAST UPDATED: 18 Sep 2006 (20060918/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

#### FILE STNGUIDE

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Sep 15, 2006 (20060915/UP).

=>

L49 FILE 'CAPLUS' ENTERED AT 13:41:35 ON 19 SEP 2006  
7 SEA ABB=ON PLU=ON (L45 OR L24) AND (L46 OR L47)

FILE 'STNGUIDE' ENTERED AT 13:42:46 ON 19 SEP 2006

L50 FILE 'CAPLUS' ENTERED AT 13:42:53 ON 19 SEP 2006  
37 SEA ABB=ON PLU=ON TAXOL/OBI AND (L46 OR L47)

FILE 'STNGUIDE' ENTERED AT 13:43:08 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 13:44:22 ON 19 SEP 2006

FILE 'CAPLUS' ENTERED AT 13:44:23 ON 19 SEP 2006  
D STAT QUE L49  
D IBIB ABS HITSTR HITIND L49 1-7

FILE 'STNGUIDE' ENTERED AT 13:46:14 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 13:47:37 ON 19 SEP 2006

L51 FILE 'CAPLUS' ENTERED AT 13:47:38 ON 19 SEP 2006  
D STAT QUE L24  
52 SEA ABB=ON PLU=ON L24 NOT L49  
D IBIB ABS HITSTR L51 1-52

FILE 'STNGUIDE' ENTERED AT 13:49:23 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 13:49:31 ON 19 SEP 2006

L52 FILE 'CAPLUS' ENTERED AT 13:49:37 ON 19 SEP 2006  
D STAT QUE L16  
D STAT QUE L45  
1 SEA ABB=ON PLU=ON L45 AND L24  
L53 0 SEA ABB=ON PLU=ON L45 AND L24 AND L49  
D IBIB ABS HITIND HITSTR L52 1

FILE 'REGISTRY' ENTERED AT 13:52:04 ON 19 SEP 2006

L54 FILE 'CAPLUS' ENTERED AT 13:52:07 ON 19 SEP 2006  
13 SEA ABB=ON PLU=ON L45 NOT L52  
D STAT QUE L54  
D IBIB ABS HITIND HITSTR L54 1-13

FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 18 SEP 2006 HIGHEST RN 907539-37-1

DICTIONARY FILE UPDATES: 18 SEP 2006 HIGHEST RN 907539-37-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

Effective September 24, 2006, Concord 3D coordinates will no longer  
be available. Please contact CAS Customer Care  
(<http://www.cas.org/supp.html>) if you have a need for 3D coordinates.



L37 774 SEA ABB=ON PLU=ON L5 NOT L36

FILE 'STNGUIDE' ENTERED AT 13:16:33 ON 19 SEP 2006  
D COST

FILE 'CAPLUS' ENTERED AT 13:19:07 ON 19 SEP 2006  
E US2003-606027/APPS

L38 1 SEA ABB=ON PLU=ON US2003-606027/AP  
D SCA  
SEL RN

FILE 'REGISTRY' ENTERED AT 13:19:45 ON 19 SEP 2006

L39 81 SEA ABB=ON PLU=ON (207680-15-7/BI OR 32981-86-5/BI OR  
352425-37-7/BI OR 352425-38-8/BI OR 352425-39-9/BI OR 352425-40  
-2/BI OR 352425-41-3/BI OR 352425-42-4/BI OR 352425-43-5/BI OR  
352425-44-6/BI OR 352425-45-7/BI OR 352425-46-8/BI OR 352425-47  
-9/BI OR 352425-48-0/BI OR 352425-49-1/BI OR 352425-50-4/BI OR  
352425-51-5/BI OR 352425-52-6/BI OR 352425-53-7/BI OR 352425-54  
-8/BI OR 352425-55-9/BI OR 352425-56-0/BI OR 352425-57-1/BI OR  
352425-58-2/BI OR 352425-59-3/BI OR 352425-60-6/BI OR 352425-61  
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352425-65-1/BI OR 352425-66-2/BI OR 352425-67-3/BI OR 352425-68  
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352426-09-6/BI OR 352426-10-9/BI OR 352426-11-0/BI OR 352426-12  
-1/BI OR 352426-13-2/BI OR 352426-14-3/BI OR 352426-15-4/BI OR  
352426-16-5/BI OR 79-03-8/BI)

L40 76 SEA ABB=ON PLU=ON L39 AND L5  
D SCA L39

FILE 'STNGUIDE' ENTERED AT 13:20:46 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 13:29:57 ON 19 SEP 2006

L41 4550 SEA ABB=ON PLU=ON 11S AND L5  
L42 6914 SEA ABB=ON PLU=ON L41 OR L8  
L43 751 SEA ABB=ON PLU=ON L5 NOT L42  
L44 51 SEA ABB=ON PLU=ON 11R AND L5  
D SCA

FILE 'CAPLUS' ENTERED AT 13:37:34 ON 19 SEP 2006

L45 14 SEA ABB=ON PLU=ON L44

FILE 'STNGUIDE' ENTERED AT 13:38:18 ON 19 SEP 2006

FILE 'CAPLUS' ENTERED AT 13:38:45 ON 19 SEP 2006

E HOLTON R/AU

L46 3 SEA ABB=ON PLU=ON HOLTON R A/AU  
L47 99 SEA ABB=ON PLU=ON HOLTON ROBER?/AU

FILE 'REGISTRY' ENTERED AT 13:40:15 ON 19 SEP 2006

L48 0 SEA ABB=ON PLU=ON L44 AND L22

FILE 'REGISTRY' ENTERED AT 11:34:17 ON 19 SEP 2006  
L10 STRUCTURE UPLOADED  
L11 50 SEA SUB=L5 SSS SAM L10

FILE 'STNGUIDE' ENTERED AT 11:35:34 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 11:36:34 ON 19 SEP 2006  
L12 STRUCTURE UPLOADED  
L13 50 SEA SUB=L5 SSS SAM L12  
D STAT QUE L11  
L14 STRUCTURE UPLOADED  
L15 0 SEA SUB=L5 SSS SAM L14  
L16 0 SEA SUB=L5 SSS FUL L14  
SAVE TEMP L16 SEA027STR14L/A  
L17 STRUCTURE UPLOADED  
L18 8 SEA SUB=L5 SSS SAM L17  
D SCA  
D STAT QUE L18  
L19 203 SEA SUB=L5 SSS FUL L17

FILE 'STNGUIDE' ENTERED AT 11:56:26 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 12:03:22 ON 19 SEP 2006  
SAVE TEMP L19 SEA027STR17L/A  
L20 STRUCTURE UPLOADED  
L21 6 SEA SUB=L5 SSS SAM L20  
D SCA  
L22 111 SEA SUB=L5 SSS FUL L20  
SAVE TEMP L22 SEA027STR22L/A  
L23 92 SEA ABB=ON PLU=ON L19 NOT L22

FILE 'CAPLUS' ENTERED AT 12:18:04 ON 19 SEP 2006  
L24 59 SEA ABB=ON PLU=ON L22

FILE 'REGISTRY' ENTERED AT 12:22:19 ON 19 SEP 2006

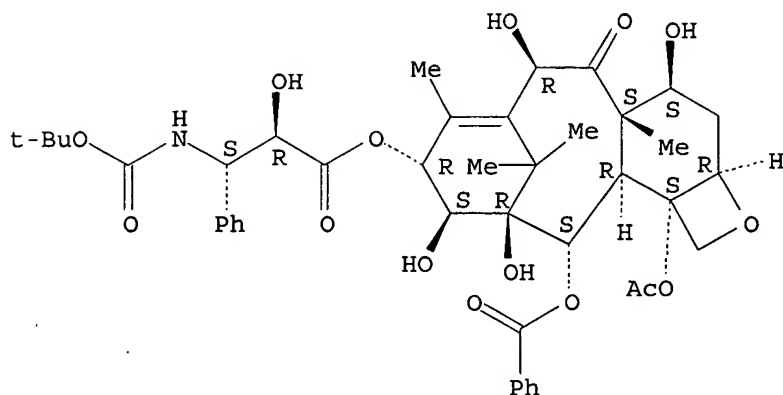
FILE 'STNGUIDE' ENTERED AT 12:27:28 ON 19 SEP 2006  
D COST

FILE 'STNGUIDE' ENTERED AT 12:27:34 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 12:35:26 ON 19 SEP 2006  
L25 101 SEA ABB=ON PLU=ON L22 AND L9  
L26 10 SEA ABB=ON PLU=ON L22 NOT L25  
L27 808 SEA ABB=ON PLU=ON L9 NOT L19  
L28 6 SEA ABB=ON PLU=ON L27 AND STEREO  
D SCA  
L29 6 SEA ABB=ON PLU=ON L9 AND STEREO

FILE 'STNGUIDE' ENTERED AT 12:42:49 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 12:56:57 ON 19 SEP 2006  
L30 STRUCTURE UPLOADED  
L31 50 SEA SUB=L5 SSS SAM L30  
L32 6747 SEA SUB=L5 SSS FUL L30  
L33 2 SEA ABB=ON PLU=ON L8 NOT L32  
D SCA  
L34 STRUCTURE UPLOADED  
L35 50 SEA SUB=L5 SSS SAM L34  
L36 6891 SEA SUB=L5 SSS FUL L34



=> d his full

(FILE 'HOME' ENTERED AT 10:32:18 ON 19 SEP 2006)

FILE 'REGISTRY' ENTERED AT 10:32:31 ON 19 SEP 2006  
L1 1 SEA ABB=ON PLU=ON TAXOL/CN  
D SCA

FILE 'CAPLUS' ENTERED AT 10:36:03 ON 19 SEP 2006  
L2 12010 SEA ABB=ON PLU=ON L1

FILE 'STNGUIDE' ENTERED AT 10:36:09 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 10:58:37 ON 19 SEP 2006

FILE 'STNGUIDE' ENTERED AT 10:59:05 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 11:00:24 ON 19 SEP 2006  
L3 STRUCTURE UPLOADED  
L4 50 SEA SSS SAM L3

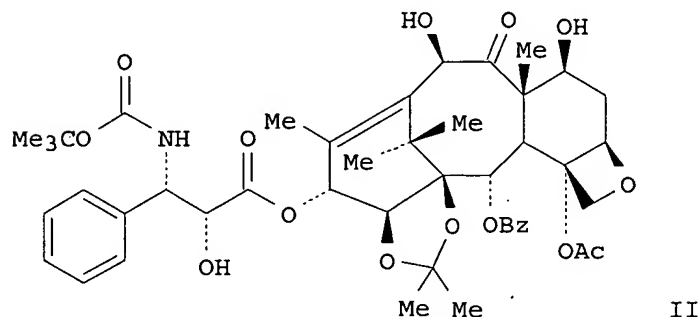
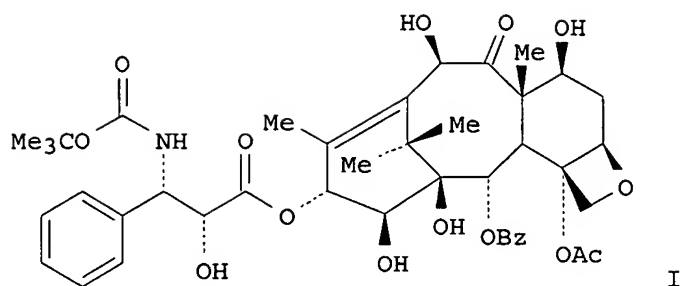
FILE 'STNGUIDE' ENTERED AT 11:03:20 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 11:06:47 ON 19 SEP 2006  
D SCA L1  
D STAT QUE L4  
L5 7665 SEA SSS FUL L3  
SAVE TEMP SEA208STR3L/A L5  
SAVE TEMP SEA027STR3L/A L5

FILE 'STNGUIDE' ENTERED AT 11:10:50 ON 19 SEP 2006

FILE 'REGISTRY' ENTERED AT 11:15:10 ON 19 SEP 2006  
L6 STRUCTURE UPLOADED  
L7 50 SEA SUB=L5 SSS SAM L6  
L8 6749 SEA SUB=L5 SSS FUL L6  
SAVE TEMP SEA027STR6L/A L8  
L9 916 SEA ABB=ON PLU=ON L5 NOT L8

FILE 'STNGUIDE' ENTERED AT 11:29:32 ON 19 SEP 2006



- AB New taxoids, 14β-hydroxydocetaxel (I) and its 1,14-acetonide II, are synthesized from 14β-hydroxy-10-deacetylbaccatin III in good yields. The cytotoxicity of the new taxoids are evaluated against different human tumor cell lines and their ability to inhibit microtubule disassembly examined 14β-Hydroxydocetaxel shows very strong cytotoxicity, especially against A549 human non-small cell lung cancer cell line (IC<sub>50</sub> = 0.8 nM).
- CC 30-20 (Terpenes and Terpenoids)  
Section cross-reference(s): 1
- IT 159143-49-4P 159143-50-7P  
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(preparation and cytotoxicity of, neoplasm inhibition in relation to)
- IT 159143-50-7P  
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(preparation and cytotoxicity of, neoplasm inhibition in relation to)
- RN 159143-50-7 CAPLUS
- CN Benzenepropanoic acid, β-[[[(1,1-dimethylethoxy)carbonyl]amino]-α-hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

e.g. I (R = Ph, Me<sub>3</sub>CO), were synthesized and evaluated as antitumor agents.

CC 30-20 (Terpenes and Terpenoids)

Section cross-reference(s): 1

IT 159143-50-7P, 14β-Hydroxytaxotere 159490-67-2P,

14β-Hydroxytaxol 159490-73-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation and neoplasm-inhibiting activity of)

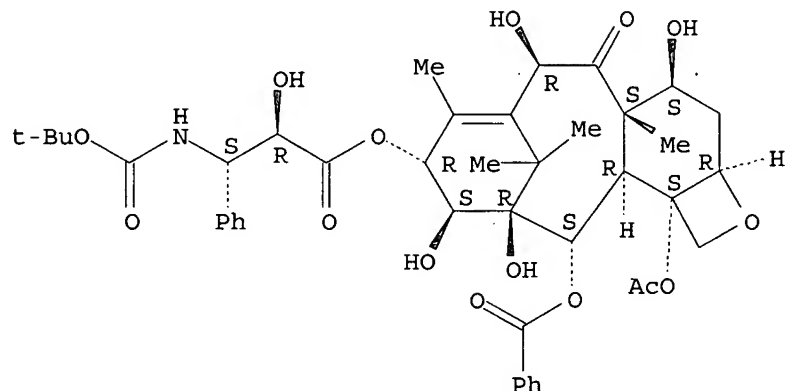
IT 159143-50-7P, 14β-Hydroxytaxotere

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation and neoplasm-inhibiting activity of)

RN 159143-50-7 CAPLUS

CN Benzenepropanoic acid, β-[[[(1,1-dimethylethoxy)carbonyl]amino]-α-hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:701098 CAPLUS

DOCUMENT NUMBER: 121:301098

TITLE: Synthesis and biological activity of 14-hydroxydocetaxel

AUTHOR(S): Ojima, Iwao; Fenoglio, Ivana; Park, Young Hoon; Pera, Paula; Bernacki, Ralph J.

CORPORATE SOURCE: Dep. Chem., State Univ. New York, Stony Brook, NY, 11794-3400, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1994), 4(13), 1571-6

CODEN: BMCLE8; ISSN: 0960-894X

DOCUMENT TYPE: Journal

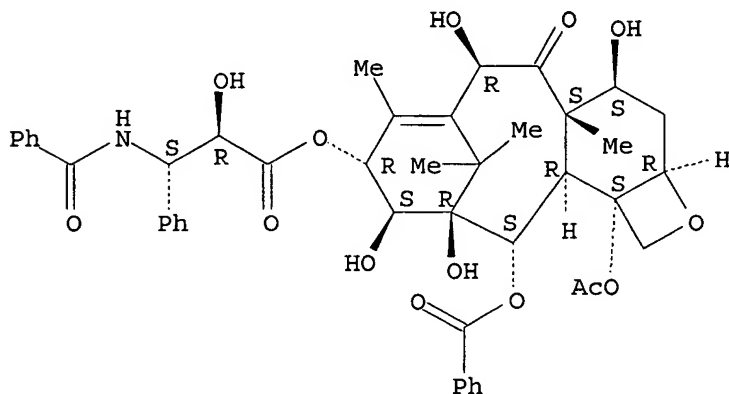
LANGUAGE: English

GI

RN 185623-21-6 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
 (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-  
 4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-  
 9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L54 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:30662 CAPLUS

DOCUMENT NUMBER: 122:10287

TITLE: Synthesis and antitumor properties of novel  
 14- $\beta$ -hydroxytaxol and related analogs

AUTHOR(S): Kant, Joydeep; Farina, Vittorio; Fairchild, Craig;  
 Kadow, John F.; Langley, David R.; Long, Byron H.;  
 Rose, William C.; Vyas, Dolatrai M.

CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Res. Inst.,  
 Wallingford, CT, 06492-7600, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1994),  
 4(13), 1565-70

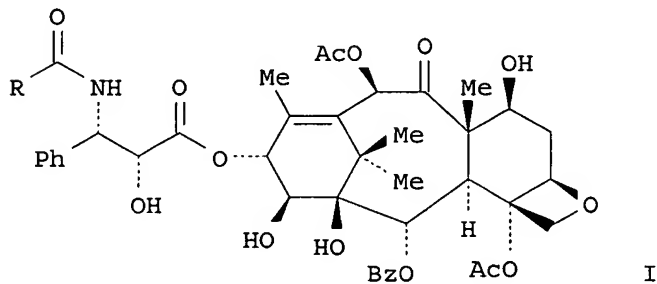
CODEN: BMCLE8; ISSN: 0960-894X

DOCUMENT TYPE: Journal

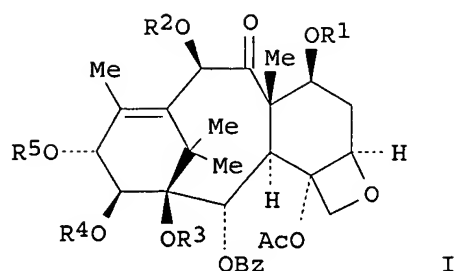
LANGUAGE: English

OTHER SOURCE(S): CASREACT 122:10287

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AB Novel analogs of TAXOL with an addnl. hydroxyl group at the C-14 position,



AB Taxane derivs. I (R1, R2, R3, R4 = independently H, alkyl, alkanoyl; R1R2, R3R4 = independently cyclic diol protecting group; R5 = H, alkyl, Ph, silyl, alkanoyl, aminoalkanoyl) were prepared from 14- $\beta$ -hydroxy-10-deacetylbaccatin III (II) for use as anticancer agents. Thus, I [R1R2 = CMe<sub>2</sub>, R3 = R4 = H, R5 = (2R,3S)-PhCH(PhCONH)CH(OH)CO] was prepared via a series of synthetic steps from II and (S,S)-PhCH(NHCOPh)CH(OH)CH:CH<sub>2</sub> and showed a 50% growth inhibition when tested against leukemia cell lines at a concns. < 0.1  $\mu$ m.

IC ICM C07D305-14

ICS C07D493-18; C07D493-08; C07D413-12; A61K031-335

CC 30-20 (Terpenes and Terpenoids)

Section cross-reference(s): 1

IT 159143-50-7P 185623-14-7P 185623-15-8P 185623-16-9P

185623-21-6P 185623-28-3P 185623-35-2P 185623-39-6P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(taxane derivs. from 14-beta-hydroxy-10 deacetylbaccatin iii)

IT 159143-50-7P 185623-21-6P

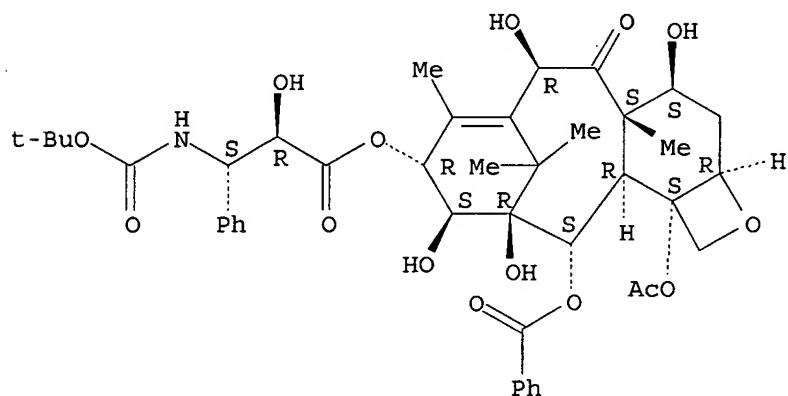
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

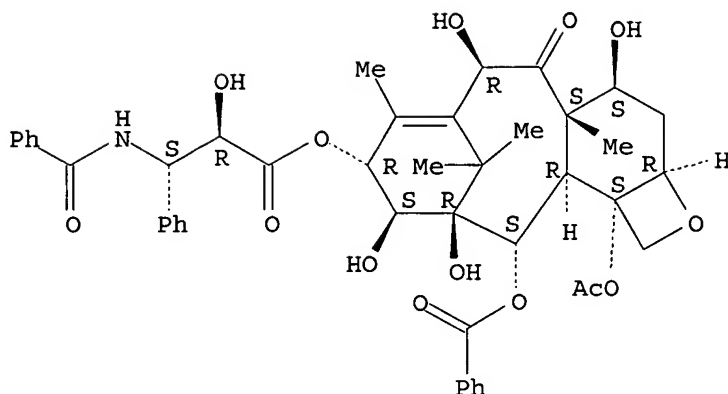
(taxane derivs. from 14-beta-hydroxy-10 deacetylbaccatin iii)

RN 159143-50-7 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:77004 CAPLUS

DOCUMENT NUMBER: 126:89601

TITLE: Preparation of taxane derivatives from 14-beta-hydroxy-10-deacetylbaccatin III

INVENTOR(S): Duvvuri, Subrahmanyam; Akella, Ventakateswarlu; Vedula, Sharma Manohar; Puranik, Ramachandra; Sattigeri, Raghavendra Madhva

PATENT ASSIGNEE(S): Dr. Reddy's Research Foundation, India

SOURCE: Eur. Pat. Appl., 32 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 747372	A1	19961211	EP 1996-304031	19960604
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IT, LI, LU, NL, PT, SE				
US 5763477	A	19980609	US 1995-471639	19950606
EP 1099696	A2	20010516	EP 2001-101809	19960604
EP 1099696	A3	20010523		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, FI				
PRIORITY APPLN. INFO.:			US 1995-471639	A 19950606
			IN 1994-681	A 19940722
			IN 1994-682	A 19940722
			IN 1994-683	A 19940722
			IN 1994-684	A 19940722
			IN 1994-685	A 19940722
			EP 1996-304031	A3 19960604

OTHER SOURCE(S): MARPAT 126:89601

GI



CC 30-20 (Terpenes and Terpenoids)  
 Section cross-reference(s): 1, 63

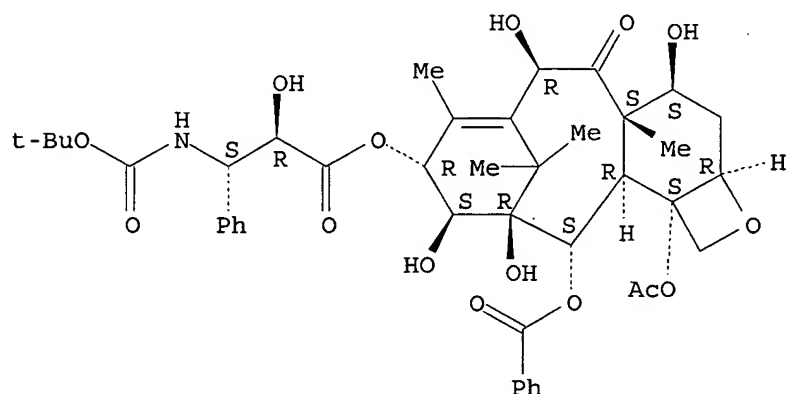
IT 156940-43-1P 156940-44-2P **159143-50-7P 185623-21-6P**  
 186348-05-0P, SB-T 101141 186348-07-2P 186348-08-3P, SB-T 10114  
 186348-09-4P, SB-T 101142 186348-10-7P, SB-T 101143 186348-11-8P, SB-T  
 101144 186348-13-0P, SB-T 101146 186348-15-2P, SB-T 101151  
 186348-23-2P, SB-T 101131 186348-24-3P, SB-T 101133 186348-25-4P, SB-T  
 101134  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation and pharmaceutical compns. of taxanes for use as antitumor  
 agents)

IT **159143-50-7P 185623-21-6P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation and pharmaceutical compns. of taxanes for use as antitumor  
 agents)

RN 159143-50-7 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]-  
 $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-  
 12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-  
 tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-  
 cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



RN 185623-21-6 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
 (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-  
 4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-  
 9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

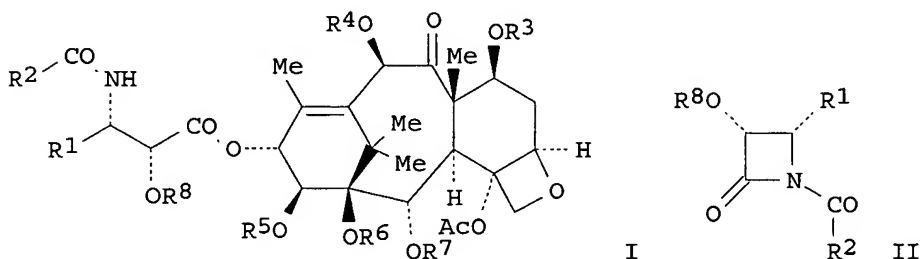
CODEN: USXXAM

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5705508	A	19980106	US 1995-542537	19951013
US 5475011	A	19951212	US 1993-40189	19930326
CA 2158147	AA	19941013	CA 1994-2158147	19940324
CA 2158147	C	19991005		
CN 1123547	A	19960529	CN 1994-192117	19940324
CN 1067682	B	20010627		
HU 73848	A2	19960930	HU 1995-2642	19940324
CZ 288924	B6	20010912	CZ 1995-2480	19940324
PT 690856	T	20030430	PT 1994-912300	19940324
ES 2190440	T3	20030801	ES 1994-912300	19940324
US 5599820	A	19970204	US 1995-461730	19950605
JP 11322737	A2	19991124	JP 1999-102935	19990409
JP 3145993	B2	20010312		

PRIORITY APPLN. INFO.:

US 1993-40189 A2 19930326  
 JP 1994-522192 A3 19940324

OTHER SOURCE(S): MARPAT 128:128162  
 GI



AB Taxanes I [R1 = alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl; R2 = alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, RO, RS, RR'N; R = R' = alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, R' = H; NRR' = nitrogen containing heterocyclyl; R3 = H, acyl, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl; R4 = H, acyl, carbamoyl, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl; R5 = R6 = H, acyl, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl; R5R6 = cyclic group such as carbonate; R7 = acyl; R8 = H, hydroxy protecting group], useful as anticancer chemotherapeutic agents, were prepared via the preparation of  $\beta$ -lactams II and their subsequent reaction with baccatin III analogs. Thus, I [R1 = R2 = Ph, R3 = R4 = R5 = R6 = R8 = H, R7 = COPh] was prepared via O-acylation of 70,100-bis(2,2,2-trichloroethyloxycarbonyl)-14-hydroxy-10-deacetylbaccatin III with II [R1 = R2 = Ph, R8 = CHMeOEt]. Prepared taxanes were tested for anticancer activity against a variety of cell lines including A121 ovarian tumor cells and HT-29 colon cancer cells.

IC ICM A61K031-445

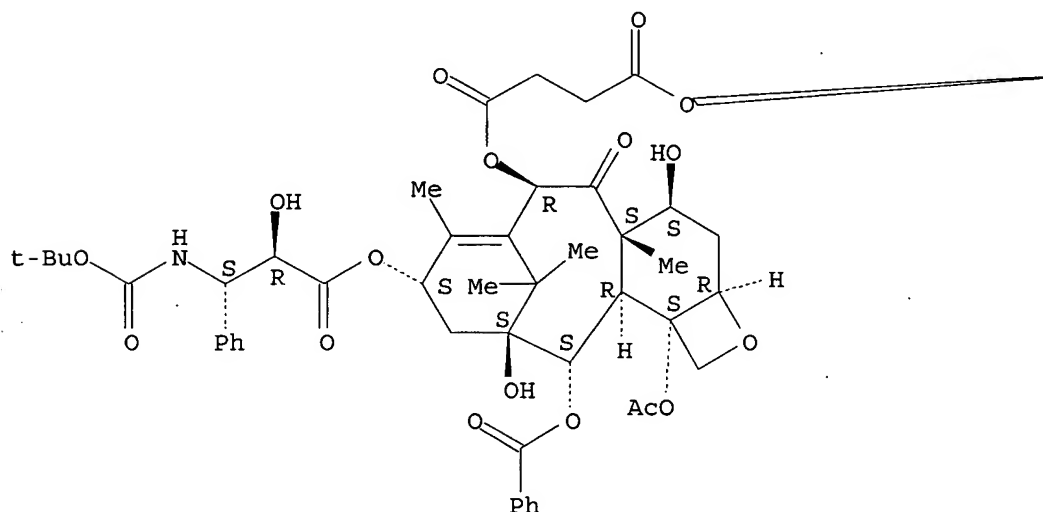
ICS C07D305-00

INCL 514320000

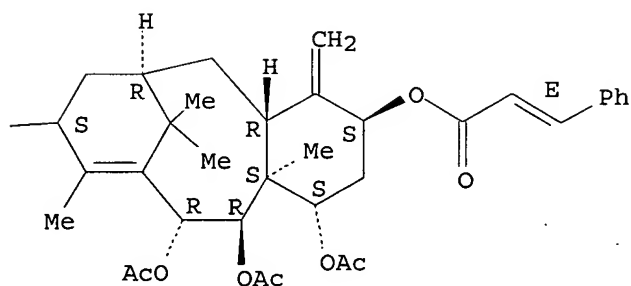
cyclodeca[3,4]benz[1,2-b]oxet-6-yl (1S,3S,4aR,6R,8S,11R,12R,12aS)-1,11,12-tris(acetyloxy)-1,2,3,4,4a,5,6,7,8,11,12,12a-dodecahydro-9,12a,13,13-tetramethyl-4-methylene-3-[[[(2E)-1-oxo-3-phenyl-2-propenyl]oxy]-6,10-methanobenzocyclodecen-8-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:41718 CAPLUS

DOCUMENT NUMBER: 128:128162

TITLE: Preparation and pharmaceutical compositions of taxanes for use as antitumor agents

INVENTOR(S): Ojima, Iwao; Bombardelli, Ezio

PATENT ASSIGNEE(S): Research Foundation of State University of New York, USA; Indena S.p.A. of Viale Ortles

SOURCE: U.S., 27 pp., Cont.-in-part of U.S. 5,475,011.

IT 237428-97-6P 237429-07-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and antitumor activity of paclitaxel(docetaxel)/2-deacetoxytaxinine J dimers)

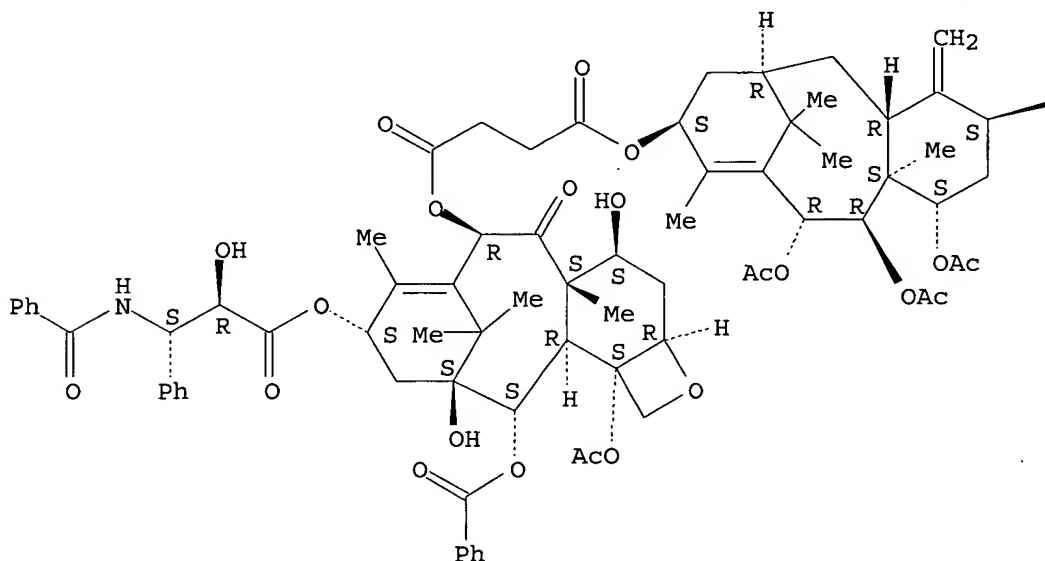
RN 237428-97-6 CAPLUS

CN Butanedioic acid, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-9-  
 [(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-6-yl  
 (1S,3S,4aR,6R,8S,11R,12R,12aS)-1,11,12-tris(acetyloxy)-  
 1,2,3,4,4a,5,6,7,8,11,12,12a-dodecahydro-9,12a,13,13-tetramethyl-4-  
 methylene-3-[[ (2E)-1-oxo-3-phenyl-2-propenyl]oxy]-6,10-  
 methanobenzocyclodecan-8-yl ester (9CI) (CA INDEX NAME)

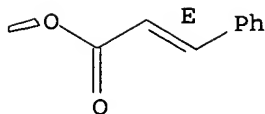
Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



RN 237429-07-1 CAPLUS

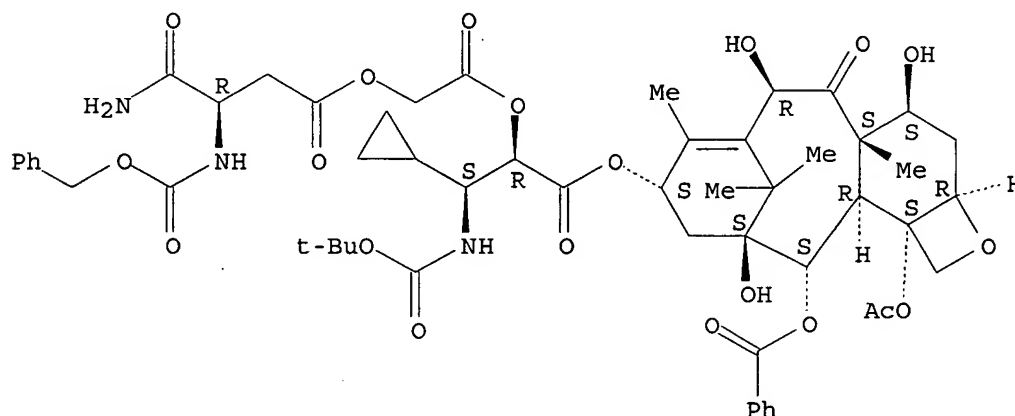
CN Butanedioic acid, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-9-[(2R,3S)-3-[[[(1,1-dimethylethoxy) carbonyl] amino]-2-hydroxy-1-oxo-3-phenylpropoxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-

3'-desphenyl-3'-cyclopropyldocetaxel)

RN 244121-78-6 CAPLUS

CN 5,8-Dioxa-2,12-diazatridecanedioic acid, 4-[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl]oxy]carbonyl]-11-(aminocarbonyl)-3-cyclopropyl-6,9-dioxo-, 1-(1,1-dimethylethyl) 13-(phenylmethyl) ester, (3S,4R,11R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:348792 CAPLUS

DOCUMENT NUMBER: 131:157845

TITLE: Chemistry and occurrence of taxane derivatives. XXXII. synthesis of paclitaxel (docetaxel)/2-deacetoxytaxinine J dimers

AUTHOR(S): Appendino, Giovanni; Belloro, Emanuela; Jakupovic, Sven; Danieli, Bruno; Jakupovic, Jasmin; Bombardelli, Ezio

CORPORATE SOURCE: Dipartimento di Scienza e Tecnologia del Farmaco, Turin, 10125, Italy

SOURCE: Tetrahedron (1999), 55(21), 6567-6576

CODEN: TETRAB; ISSN: 0040-4020

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Starting from taxanes available in multigram amts. from widespread ornamental yews (10-deacetylbaicatin III and 2'-deacetoxyaustrospicatin), two dimeric taxoids with potential dual target specificity ( $\beta$ -tubulin and P-gp) were synthesized. Both compds. lacked significant cytotoxicity, though one retained a strong activity in the tubulin depolymn. assay.

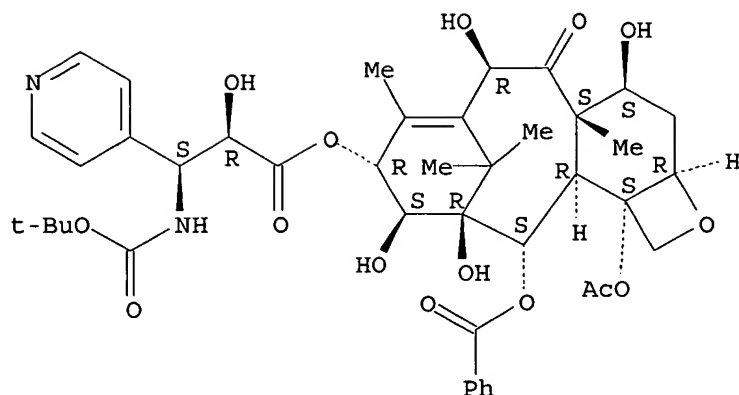
CC 30-20 (Terpenes and Terpenoids)

Section cross-reference(s): 1

IT 237428-97-6P 237429-07-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and antitumor activity of paclitaxel(docetaxel)/2-deacetoxytaxinine J dimers)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:404096 CAPLUS

DOCUMENT NUMBER: 131:243428

TITLE: Synthesis and evaluation of novel water-soluble prodrugs of a 3'-desphenyl-3'-cyclopropyl analogue of docetaxel

AUTHOR(S): Yamaguchi, Tetsuo; Harada, Naoyuki; Ozaki, Kunihiro; Arakawa, Hiroaki; Oda, Kouji; Nakanishi, Noriyuki; Tsujihara, Kenji; Hashiyama, Tomiki

CORPORATE SOURCE: Medicinal Chemistry Research Laboratories, Tanabe Seiyaku Co., Ltd., Toda, 335-8505, Japan

SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(12), 1639-1644

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A novel 3'-desphenyl-3'-cyclopropyl analog of docetaxel was synthesized from 10-deacetyl-baccatin III. The cytotoxicity of the new taxoid was evaluated against several human tumor cell lines, and it had ca. 20 times stronger activity against human colon cancer cell lines (WiDr and Colon 320) than that of docetaxel. This taxoid was converted to its water-soluble prodrugs that have 2'-substituted amino acid derivs. with spacer. The prodrugs had good solubility in saline and showed more potent antitumor activity against B 16 melanoma in mice than that of docetaxel.

CC 30-20 (Terpenes and Terpenoids)

Section cross-reference(s): 1

IT 178247-80-8P 178247-81-9P 178247-82-0P 178247-83-1P 178247-84-2P  
178247-85-3P 178247-87-5P 178247-97-7P 178248-33-4P 178248-34-5P  
178248-35-6P 178248-38-9P 205640-20-6P **244121-78-6P**  
244121-79-7P 244121-80-0P 244121-81-1P 244121-82-2P 244121-83-3P  
244121-84-4P

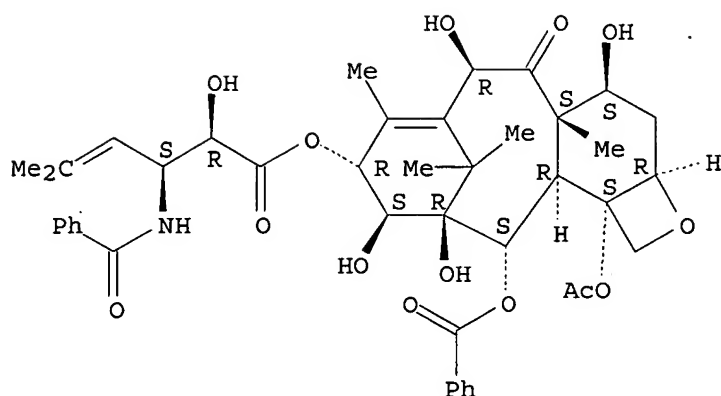
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and antitumor activity of water-soluble prodrugs of 3'-desphenyl-3'-cyclopropyldocetaxel)

IT **244121-78-6P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

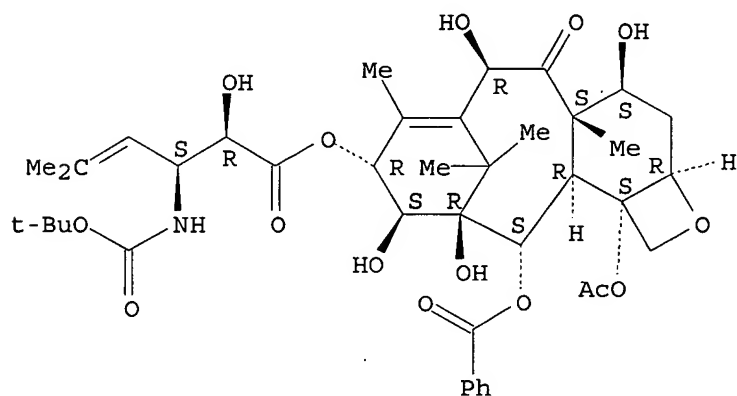
(synthesis and antitumor activity of water-soluble prodrugs of



RN 232948-86-6 CAPLUS

CN 4-Hexenoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

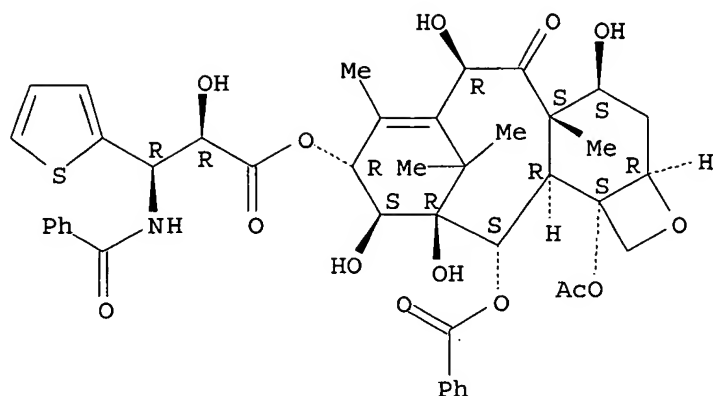
Absolute stereochemistry.



RN 232948-87-7 CAPLUS

CN 4-Pyridinepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)

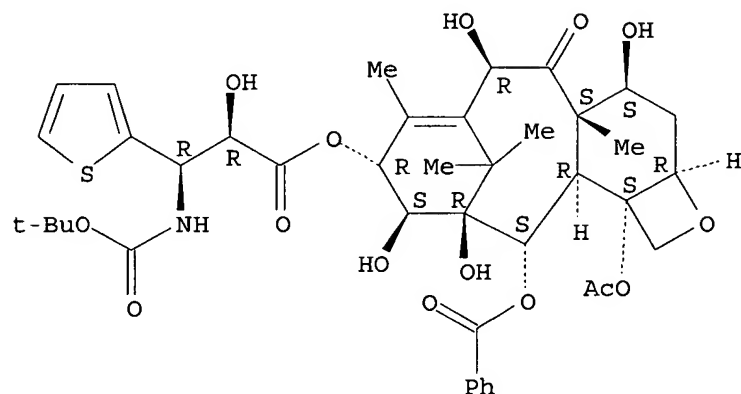
Absolute stereochemistry.



RN 232948-84-4 CAPLUS

CN 2-Thiophenepropanoic acid, β-[[[(1,1-dimethylethoxy)carbonyl]amino]-α-hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

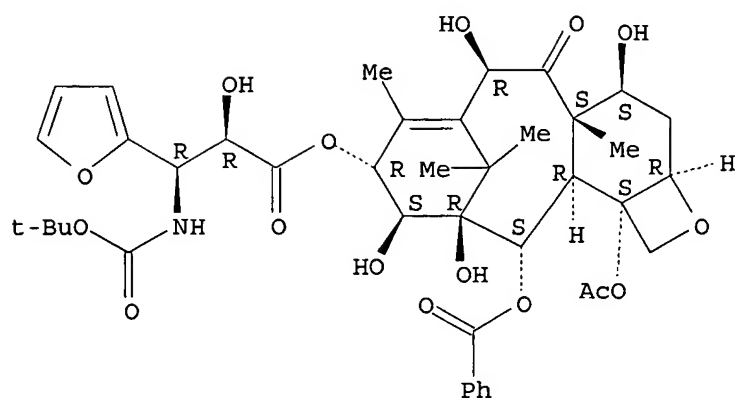


RN 232948-85-5 CAPLUS

CN 4-Hexenoic acid, 3-(benzoylamino)-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

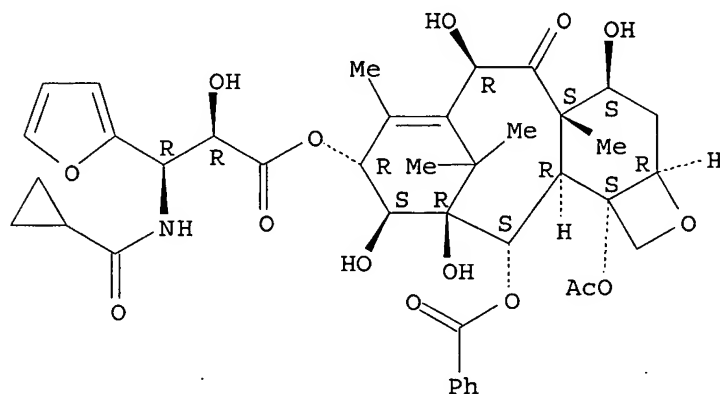




RN 232948-82-2 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -[(cyclopropylcarbonyl)amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ R)-(9CI) (CA INDEX NAME)

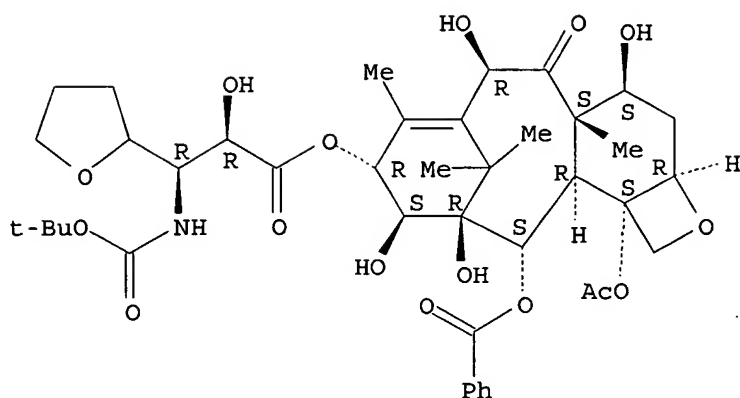
Absolute stereochemistry.



RN 232948-83-3 CAPLUS

CN 2-Thiophenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ R)-(9CI) (CA INDEX NAME)

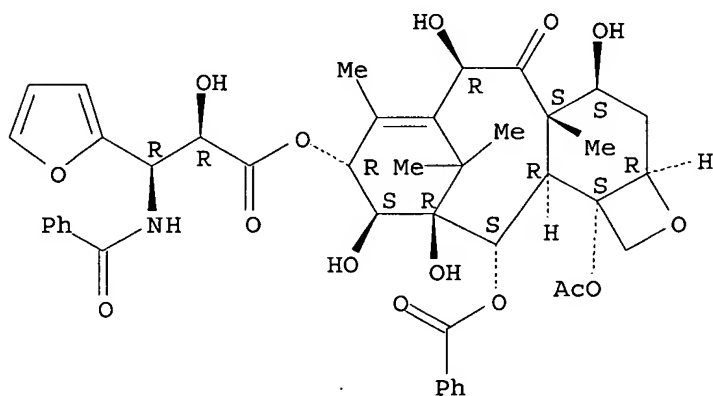
Absolute stereochemistry.



RN 232948-80-0 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ R)-(9CI) (CA INDEX NAME)

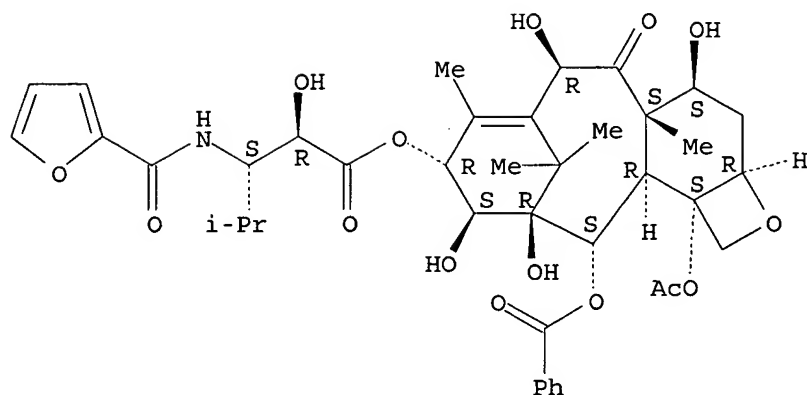
Absolute stereochemistry.



RN 232948-81-1 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ R)-(9CI) (CA INDEX NAME)

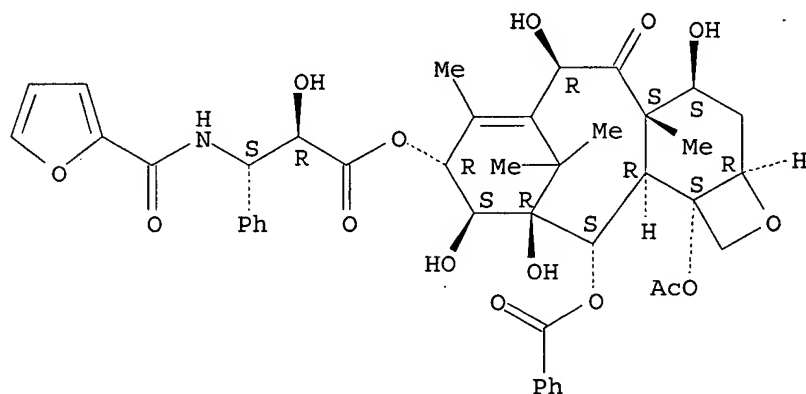
Absolute stereochemistry.



RN 232948-78-6 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[(2-furanylcarbonyl)amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)-(9CI) (CA INDEX NAME)

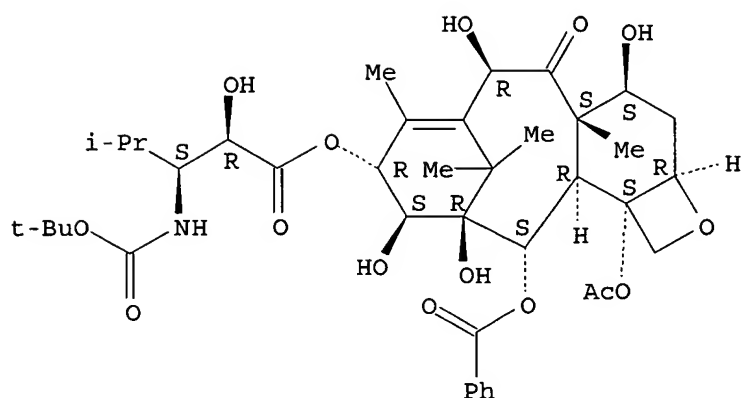
Absolute stereochemistry.



RN 232948-79-7 CAPLUS

CN L-threo-Heptonic acid, 4,7-anhydro-3,5,6-trideoxy-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester (9CI) (CA INDEX NAME)

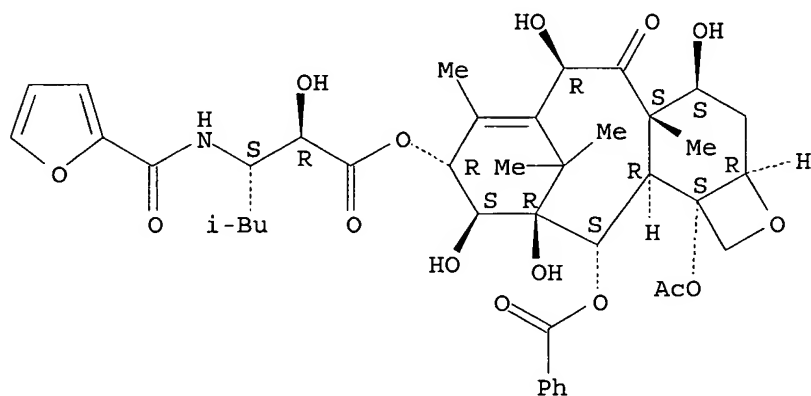
Absolute stereochemistry.



RN 232948-76-4 CAPLUS

CN Hexanoic acid, 3-[(2-furanylcarbonyl)amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

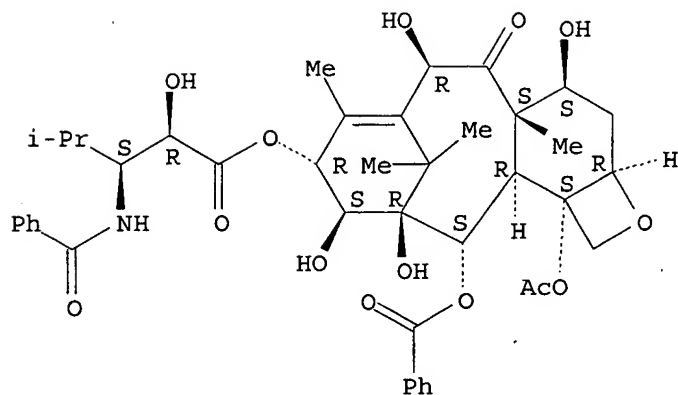
Absolute stereochemistry.



RN 232948-77-5 CAPLUS

CN L-threo-Pentonic acid, 3,4,5-trideoxy-3-[(2-furanylcarbonyl)amino]-4-methyl-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester (9CI) (CA INDEX NAME)

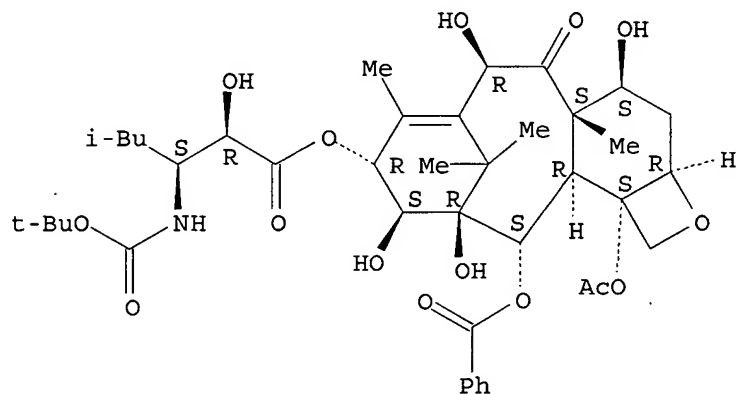
Absolute stereochemistry.



RN 232948-74-2 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

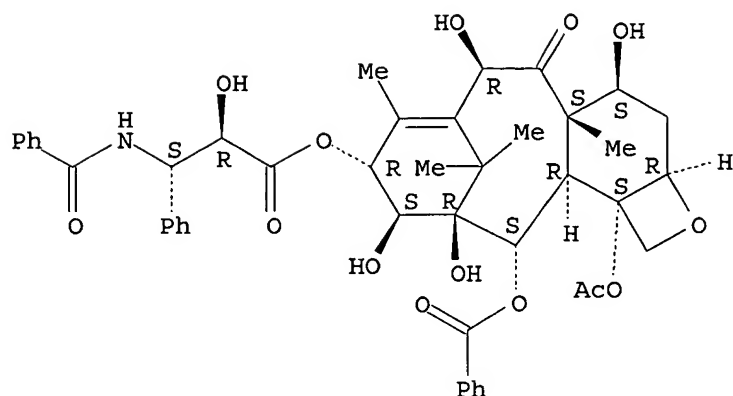
Absolute stereochemistry.



RN 232948-75-3 CAPLUS

CN L-threo-Pentonic acid, 3,4,5-trideoxy-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester (9CI) (CA INDEX NAME)

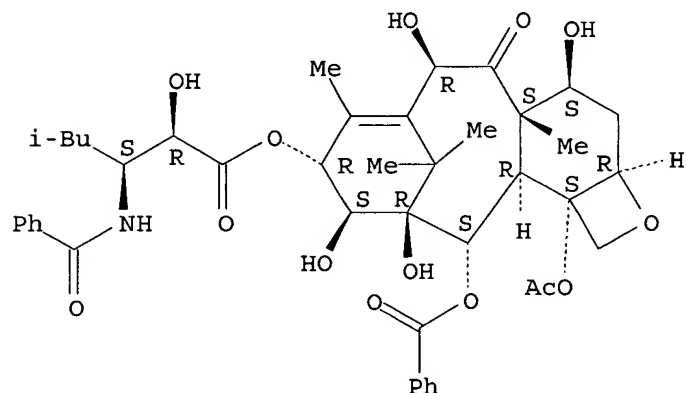
Absolute stereochemistry.



RN 232948-71-9 CAPLUS

CN Hexanoic acid, 3-(benzoylamino)-2-hydroxy-5-methyl-,  
(2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-  
4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-  
9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

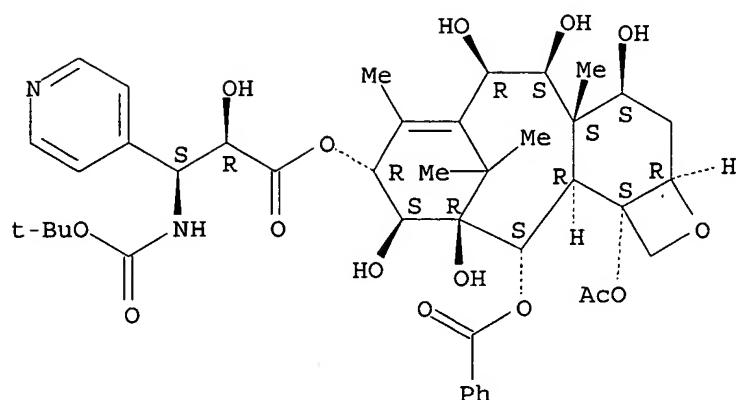
Absolute stereochemistry.



RN 232948-72-0 CAPLUS

CN L-threo-Pentonic acid, 3-(benzoylamino)-3,4,5-trideoxy-4-methyl-,  
(2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-  
4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-  
9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 159143-50-7 185623-21-6 232948-71-9  
 232948-72-0 232948-74-2 232948-75-3  
 232948-76-4 232948-77-5 232948-78-6  
 232948-79-7 232948-80-0 232948-81-1  
 232948-82-2 232948-83-3 232948-84-4  
 232948-85-5 232948-86-6 232948-87-7

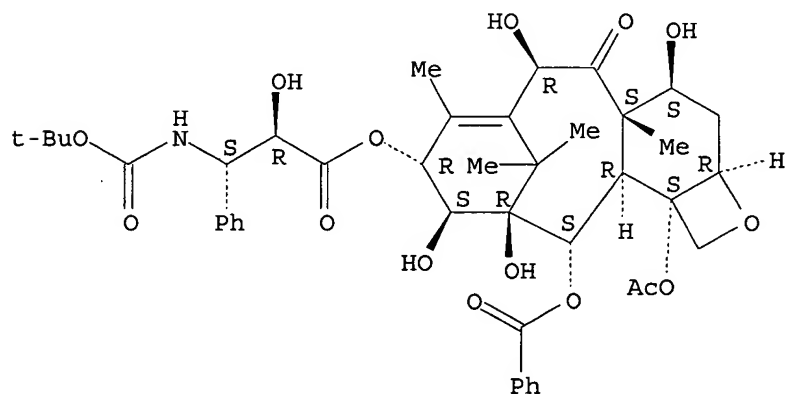
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of novel water soluble taxane diterpenes as anticancer agents)

RN 159143-50-7 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)

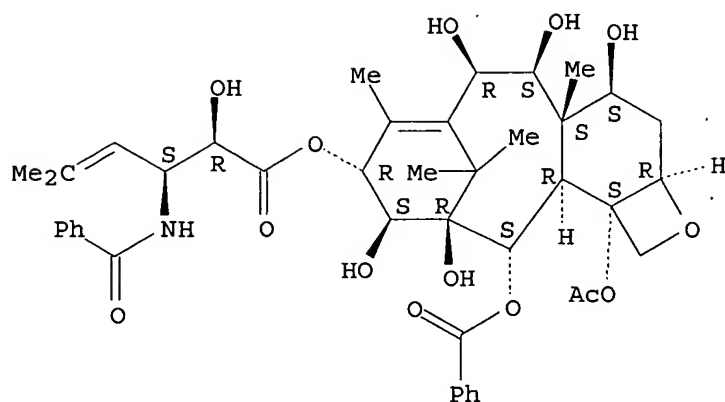
Absolute stereochemistry.



RN 185623-21-6 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)

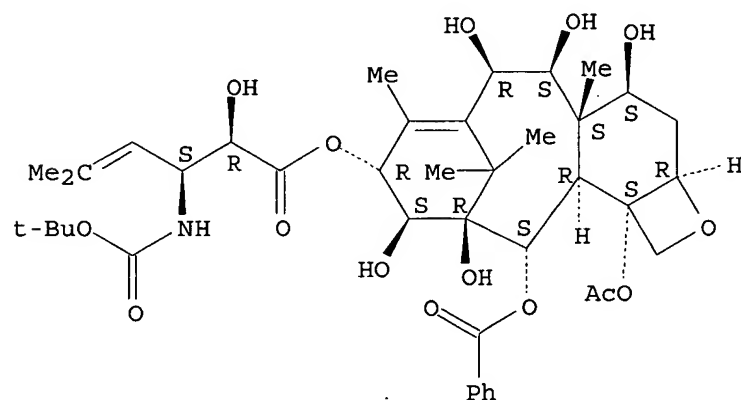
Absolute stereochemistry. Rotation (-).



RN 232948-51-5 CAPLUS

CN 4-Hexenoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

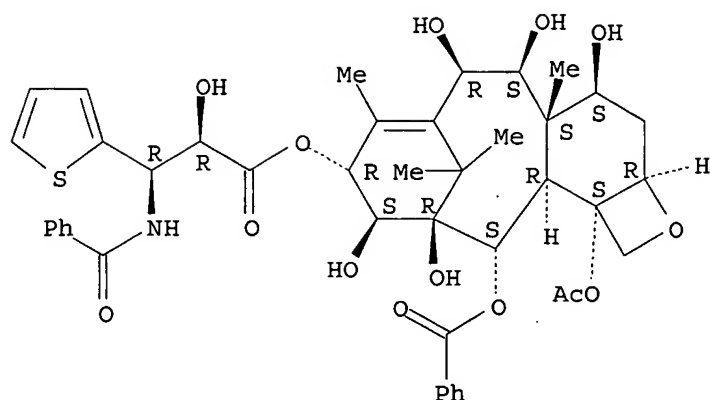


RN 232948-52-6 CAPLUS

CN 4-Pyridinepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

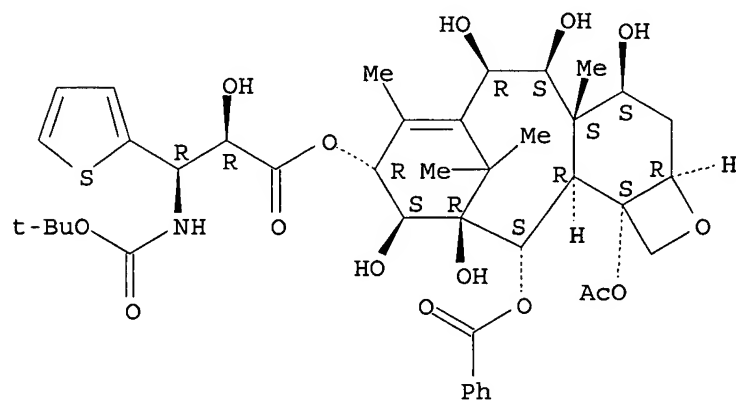




RN 232948-49-1 CAPLUS

CN 2-Thiophenepropanoic acid, β-[[[(1,1-dimethylethoxy)carbonyl]amino]-α-hydroxy-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βR)-(9CI) (CA INDEX NAME)

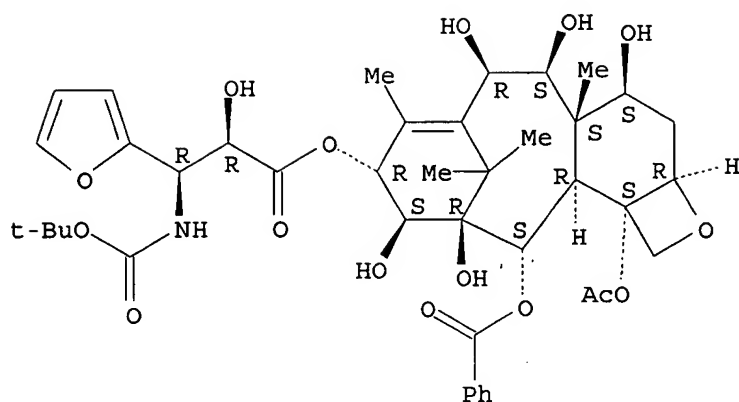
Absolute stereochemistry.



RN 232948-50-4 CAPLUS

CN 4-Hexenoic acid, 3-(benzoylamino)-2-hydroxy-5-methyl-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)-(9CI) (CA INDEX NAME)

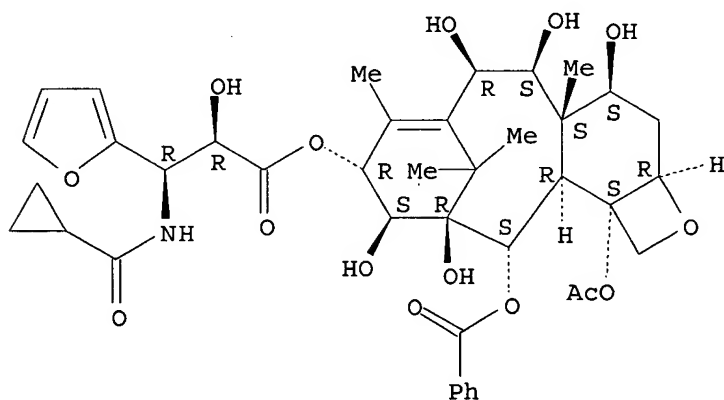
Absolute stereochemistry.



RN 232948-47-9 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -[(cyclopropylcarbonyl)amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ R)-(9CI) (CA INDEX NAME)

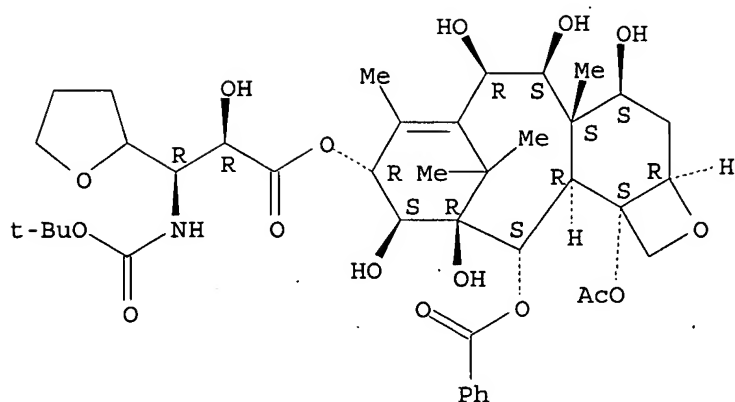
Absolute stereochemistry.



RN 232948-48-0 CAPLUS

CN 2-Thiophenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ R)-(9CI) (CA INDEX NAME)

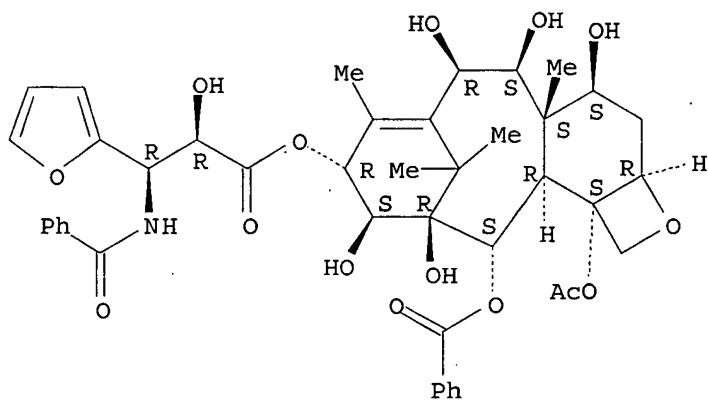
Absolute stereochemistry.



RN 232948-45-7 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ R)- (9CI) (CA INDEX NAME)

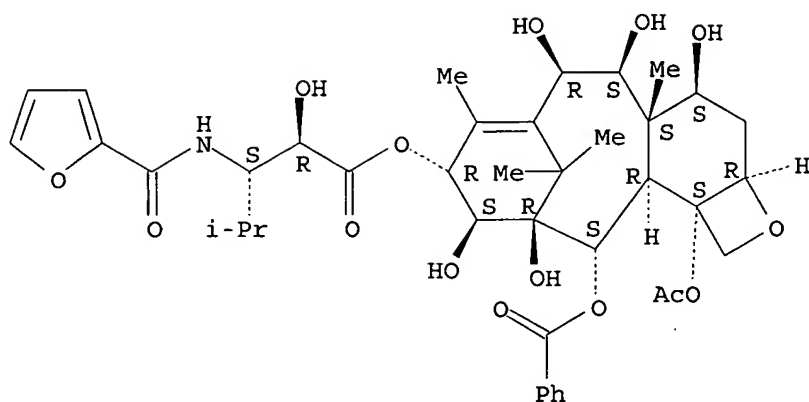
Absolute stereochemistry.



RN 232948-46-8 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ R)- (9CI) (CA INDEX NAME)

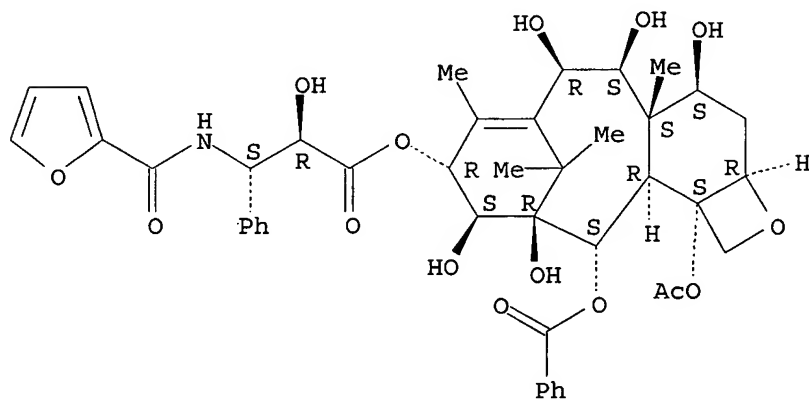
Absolute stereochemistry.



RN 232948-43-5 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[(2-furanylcarbonyl)amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)-(9CI) (CA INDEX NAME)

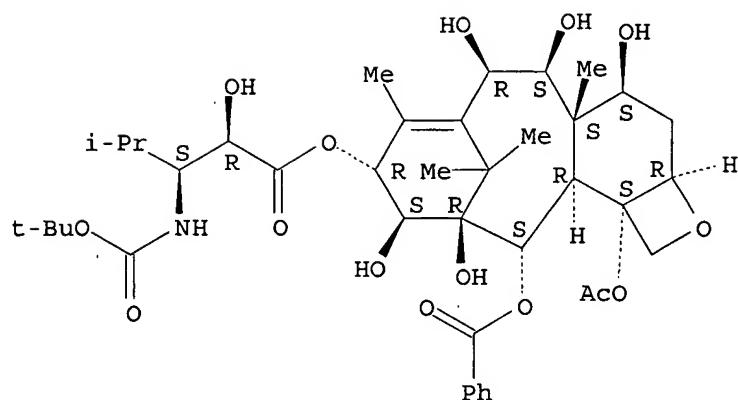
Absolute stereochemistry.



RN 232948-44-6 CAPLUS

CN L-threo-Heptonic acid, 4,7-anhydro-3,5,6-trideoxy-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (4 $\xi$ )-(9CI) (CA INDEX NAME)

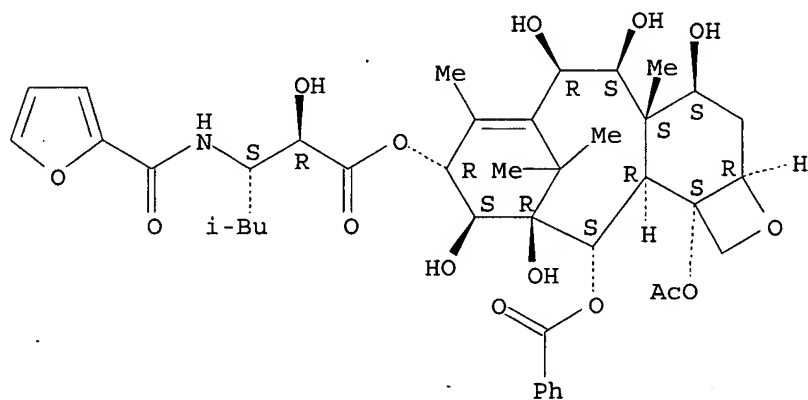
Absolute stereochemistry.



RN 232948-40-2 CAPLUS

CN Hexanoic acid, 3-[(2-furanylcarbonyl)amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

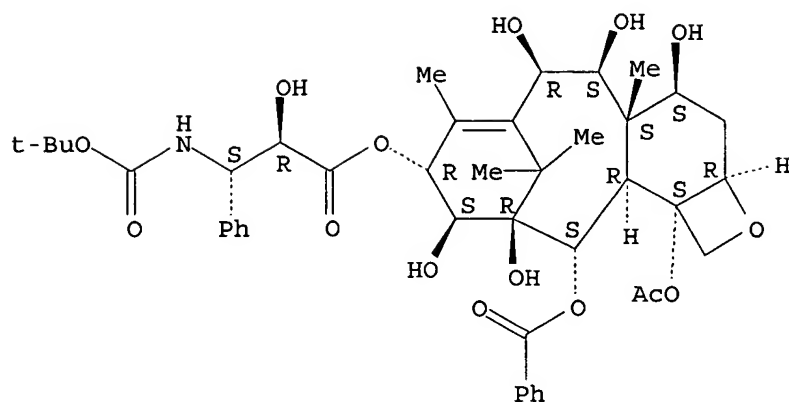
Absolute stereochemistry.



RN 232948-41-3 CAPLUS

CN L-threo-Pentonic acid, 3,4,5-trideoxy-3-[(2-furanylcarbonyl)amino]-4-methyl-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester (9CI) (CA INDEX NAME)

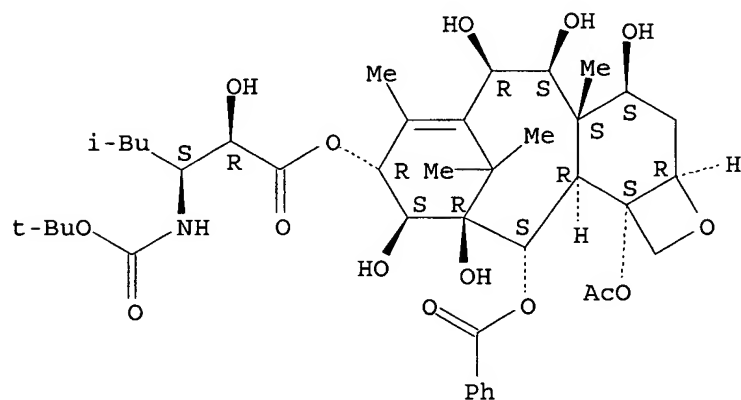
Absolute stereochemistry.



RN 232948-38-8 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



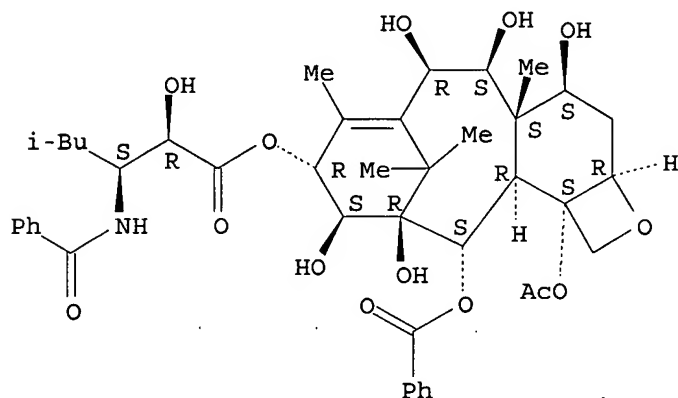
RN 232948-39-9 CAPLUS

CN L-threo-Pentonic acid, 3,4,5-trideoxy-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CN Hexanoic acid, 3-(benzoylamino)-2-hydroxy-5-methyl-,  
(2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-  
(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-  
pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-  
b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

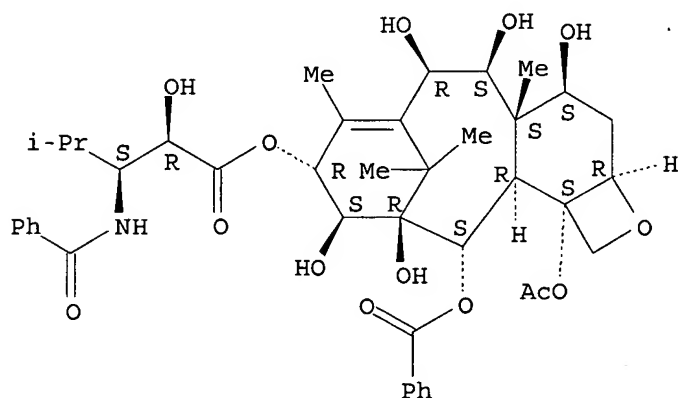
Absolute stereochemistry.



RN 232948-36-6 CAPLUS

CN L-threo-Pentonic acid, 3-(benzoylamino)-3,4,5-trideoxy-4-methyl-,  
(2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-  
(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-  
pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-  
b]oxet-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 232948-37-7 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-  
 $\alpha$ -hydroxy-, (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-  
(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-  
4,5,6,10,11-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-  
cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

232948-58-2P 232948-59-3P 232948-60-6P 232948-61-7P 232948-62-8P  
 232948-63-9P 232948-64-0P 232948-65-1P 232948-66-2P 232948-67-3P  
 232948-68-4P 232948-69-5P 232948-70-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of novel water soluble taxane diterpenes as anticancer agents)

IT 1191-15-7, Diisobutylaluminum hydride 7784-21-6, Aluminum hydride  
 13813-25-7, Samarium iodide 16940-66-2, Sodium borohydride 16949-15-8,  
 Lithium borohydride 25895-60-7, Sodium cyanoborohydride 33725-74-5,  
 Tetrabutylammonium borohydride 156940-43-1 156940-44-2  
 159143-50-7 185623-21-6 186348-06-1 186348-08-3  
 186348-22-1 232948-71-9 232948-72-0  
 232948-74-2 232948-75-3 232948-76-4  
 232948-77-5 232948-78-6 232948-79-7  
 232948-80-0 232948-81-1 232948-82-2  
 232948-83-3 232948-84-4 232948-85-5  
 232948-86-6 232948-87-7 232948-88-8 232948-89-9  
 232948-90-2 232948-91-3 232948-92-4 232948-93-5 232948-94-6  
 232948-95-7 232948-96-8 232948-97-9 232948-98-0 232949-00-7  
 232949-01-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of novel water soluble taxane diterpenes as anticancer agents)

IT 232948-34-4P, 10-Deacetyl-9-deketo-9 $\beta$ ,14 $\beta$ -  
 dihydroxypaclitaxel 232948-35-5P 232948-36-6P  
 232948-37-7P 232948-38-8P 232948-39-9P  
 232948-40-2P 232948-41-3P 232948-43-5P  
 232948-44-6P 232948-45-7P 232948-46-8P  
 232948-47-9P 232948-48-0P 232948-49-1P  
 232948-50-4P 232948-51-5P 232948-52-6P

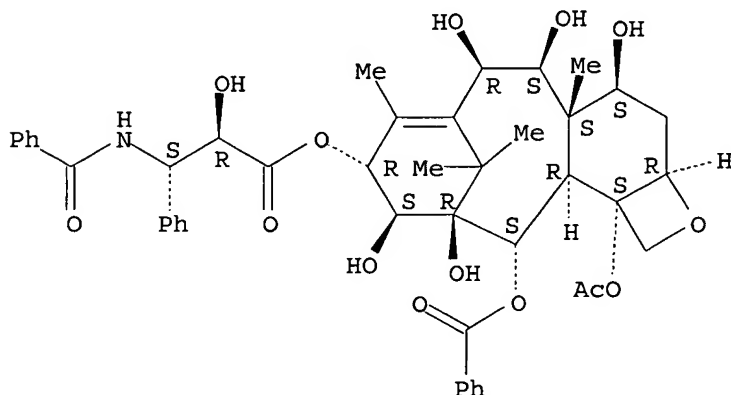
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of novel water soluble taxane diterpenes as anticancer agents)

RN 232948-34-4 CAPLUS

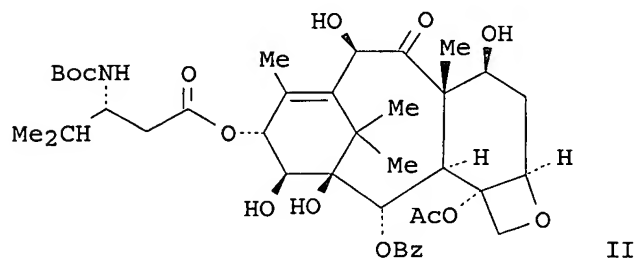
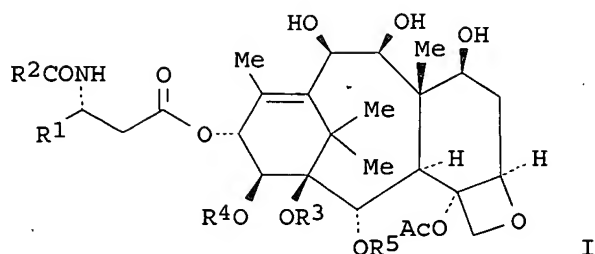
CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
 (2aR,4S,4aS,5S,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-  
 (benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,6,10,11-  
 pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-  
 b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 232948-35-5 CAPLUS





AB The present invention relates to novel taxane terpene compds. I [R1 = (un)substituted, straight or branched alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, cycloalkenyl or heterocycloalkenyl; R2 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl or heteroaryl, RO-, RS- or RR6N-; R = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl or heteroaryl; R6 = H, R; RR6 together form a cyclic structure; R3 = H, acyl, alkyl, alkenyl, alkynyl, (un)substituted cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl or a hydroxy protecting group; R4 = H, acyl, alkyl, alkenyl, alkynyl, (un)substituted cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, or a hydroxy protecting group; R3R4 together form cyclic carbonate, cyclic thiocarbonate or acetonide structure; R5 = aryl] useful as anti-cancer agents and to a process for preparing I. Thus, I (R1 = CHMe2, R2 = OCMe3, R3 = R4 = H, R5 = Ph) was prepared in 75% yield via reduction of 10-deacetyl-14 $\beta$ -hydroxypaclitaxel (II) with samarium iodide in aqueous THF. I (R1 = CHMe2, R2 = OCMe3, R3 = R4 = H, R5 = Ph) was tested for water solubility (0.2214 mg/mL) and antitumor activity [ED50(test compound)/ED50(paclitaxel) = 4 (A549 cancer cell line); ED50(test compound)/ED50(paclitaxel) = 8.2 (SKOV-3 cancer cell line); ED50(test compound)/ED50(paclitaxel) = 5.5 (SK-MEL-2 cancer cell line); ED50(test compound)/ED50(paclitaxel) = 3.1 (HCT15 cancer cell line); ED50(test compound)/ED50(paclitaxel) = 1.0 (XF498 cancer cell line)].

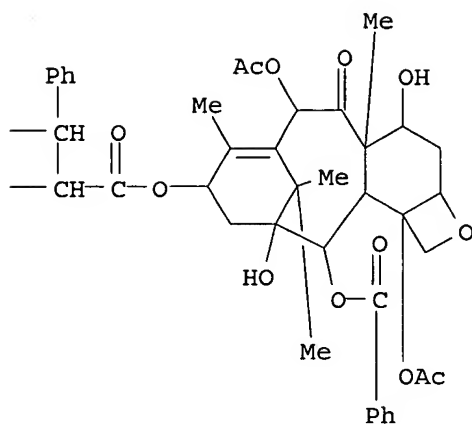
IC ICM C07D305-14

CC 30-20 (Terpenes and Terpenoids)

Section cross-reference(s): 1

IT 33069-62-4DP; Paclitaxel, analogs 114977-28-5DP, Docetaxel, analogs, 232948-34-4P, 10-Deacetyl-9-deketo-9 $\beta$ ,14 $\beta$ -dihydroxypaclitaxel 232948-35-5P 232948-36-6P 232948-37-7P 232948-38-8P 232948-39-9P 232948-40-2P 232948-41-3P 232948-43-5P 232948-44-6P 232948-45-7P 232948-46-8P 232948-47-9P 232948-48-0P 232948-49-1P 232948-50-4P 232948-51-5P 232948-52-6P 232948-53-7P 232948-54-8P 232948-55-9P 232948-56-0P 232948-57-1P

PAGE 1-B



L54 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:487282 CAPLUS

DOCUMENT NUMBER: 131:116387

TITLE: Preparation of novel water soluble taxane diterpenes as anticancer agents

INVENTOR(S): Chai, Ki Byung; Moon, Young Ho; Kim, Nam Du; Ha, Tae Hee; Shin, Jung Ae; Lim, Chang Gi; Kim, Wan Joo; Lee, Gwan Sun; Suh, Kwee Hyun

PATENT ASSIGNEE(S): Hanmi Pharmaceutical Co., Ltd., S. Korea

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937631	A1	19990729	WO 1999-KR39	19990125
W: AU, CA, CN, JP, RU, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9921877	A1	19990809	AU 1999-21877	19990125
PRIORITY APPLN. INFO.:			KR 1998-2430	A 19980126
			WO 1999-KR39	W 19990125
OTHER SOURCE(S):			CASREACT 131:116387; MARPAT 131:116387	
GI				

animals. Thus, steroid-containing macrolide glycopeptide I was prepared as as carriers for steroid/non-steroid anti-inflammatory, antineoplastic, and antiviral active mol. The compds. demonstrating a 30% or higher inhibition of TNF- $\alpha$  production at a dose of 10 mg/kg are considered active. The compds. demonstrating the same or better analgesic activity in mice than acetyl salicylic acid are considered active. In vitro assay for antineoplastic activity and inhibitory effect on HIV replication are reported.

IC ICM C07J

CC 33-7 (Carbohydrates)

Section cross-reference(s): 1, 32, 34, 63

IT 641630-46-8P 641630-48-0P 641630-49-1P 641630-50-4P 641630-51-5P  
641630-52-6P 641630-53-7P 641630-54-8P 641630-55-9P 641630-56-0P  
641630-57-1P 641630-58-2P 641630-59-3P 641630-60-6P 641630-61-7P  
641630-62-8P 641630-63-9P 641630-64-0P 641630-65-1P  
641630-66-2P 641630-67-3P 642087-21-6P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of steroid-containing macrolide glycopeptides as carriers for steroid/non-steroid anti-inflammatory, antineoplastic, and antiviral active mols.)

IT 641630-65-1P

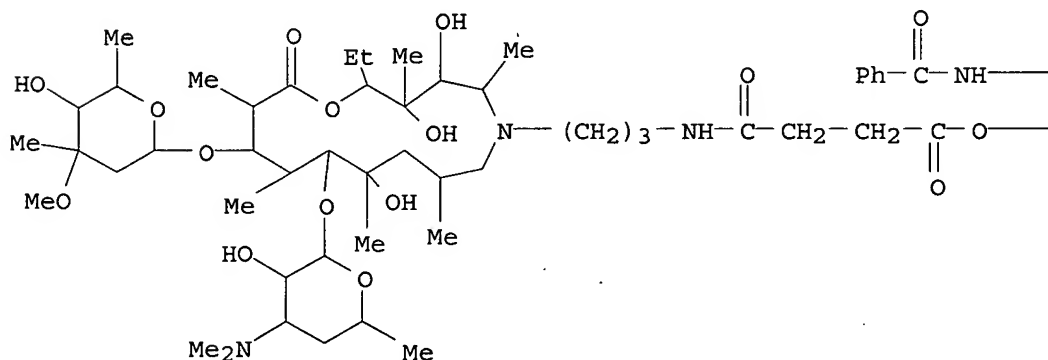
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of steroid-containing macrolide glycopeptides as carriers for steroid/non-steroid anti-inflammatory, antineoplastic, and antiviral active mols.)

RN 641630-65-1 CAPLUS

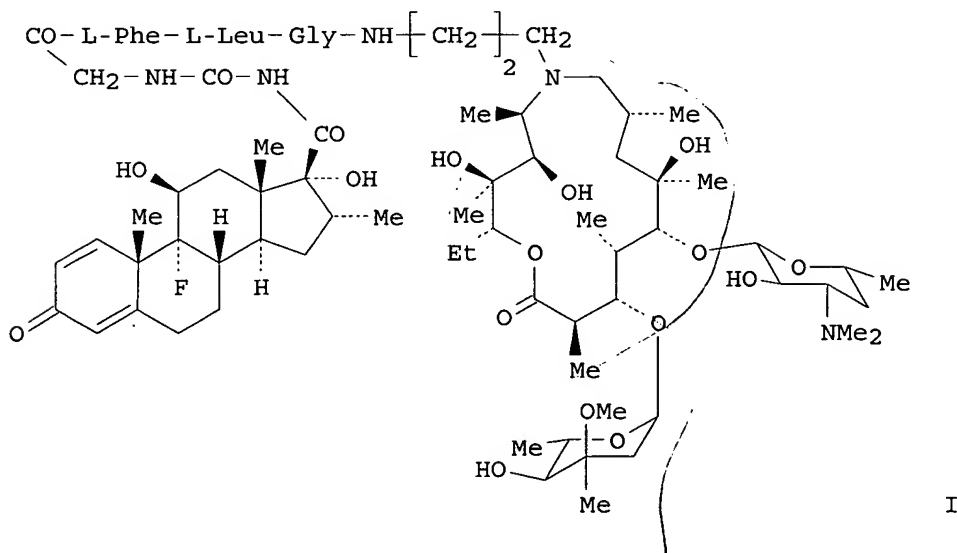
CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -[4-[[3-[(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-13-[(2,6-dideoxy-3-C-methyl-3-O-methyl- $\alpha$ -L-ribo-hexopyranosyl)oxy]-2-ethyl-3,4,10-trihydroxy-3,5,8,10,12,14-hexamethyl-15-oxo-11-[[3,4,6-trideoxy-3-(dimethylamino)- $\beta$ -D-xylo-hexopyranosyl]oxy]-1-oxa-6-azacyclopentadec-6-yl]propyl]amino]-1,4-dioxobutoxy]-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-3,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)

PAGE 1-A

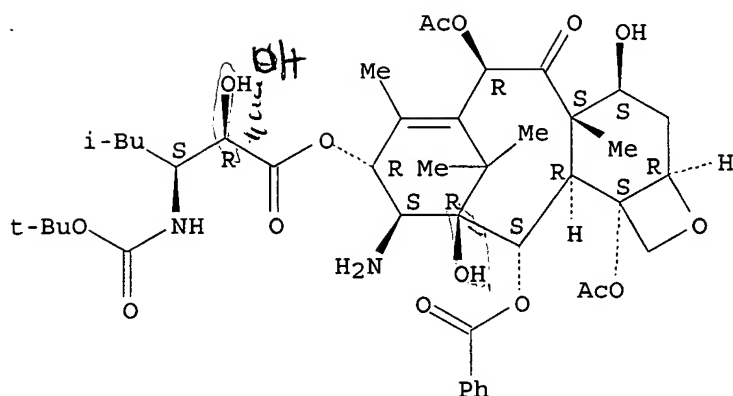


## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005313	A2	20040115	WO 2003-IB3792	20030708
WO 2004005313	A3	20050421		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003264917	A1	20040123	AU 2003-264917	20030708
US 2004077612	A1	20040422	US 2003-616046	20030708
EP 1551865	A2	20050713	EP 2003-762853	20030708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1665831	A	20050907	CN 2003-816097	20030708
JP 2005538070	T2	20051215	JP 2004-519131	20030708
NO 2005000575	A	20050315	NO 2005-575	20050202
PRIORITY APPLN. INFO.:			US 2002-395190P	P 20020708
			WO 2003-IB3792	W 20030708
OTHER SOURCE(S):		MARPAT 140:94230		
GI				



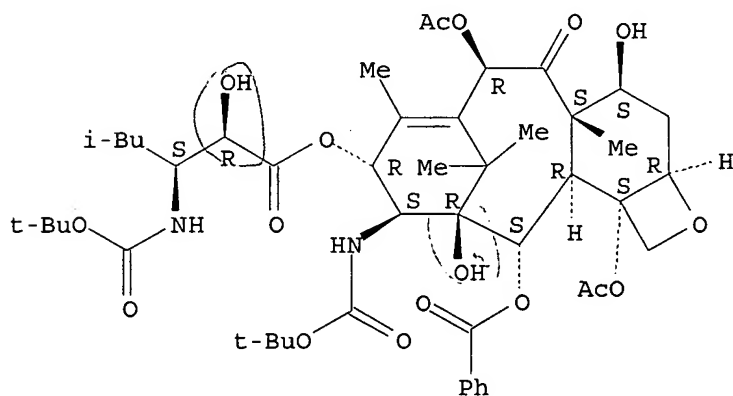
AB The present invention relates (a) to new compds. represented by formula M-L-V; wherein M represents a macrolide moiety derived from macrolide possessing the property of accumulation in inflammatory cells, V represents and ant-inflammatory steroid or nonsteroid subunit, or an antineoplastic or antiviral subunit and L represents a linking group covalently linking M and V; (b) to their pharmacol. acceptable salts, prodrugs and solvates, (c) to processes and intermediates for their preparation, and (d) to their use in the treatment of inflammatory/neoplastic/viral diseases and conditions in humans and



RN 675584-63-1 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy) carbonyl] amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-10-[[[(1,1-dimethylethoxy) carbonyl] amino]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:41493 CAPLUS

DOCUMENT NUMBER: 140:94230

TITLE: Preparation of steroid-containing macrolide glycopeptides as carriers for steroid/non-steroid anti-inflammatory, antineoplastic, and antiviral active molecules

INVENTOR(S): Mercep, Mladen; Mesic, Milan; Tomaskovic, Linda; Markovic, Stribor

PATENT ASSIGNEE(S): Pliva D.D., Croatia; Pliva - Istrazivacki Institut D.O.O.

SOURCE: PCT Int. Appl., 96 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

acyl, hydroxyaminoacyl], from 13-ketobaccatin derivs. II via functionalization at the 14-position. Thus, preparation of taxane derivative I [XR4 = NHCO; R1 = TES; R2 = Ac; R6 = C6H5; R9 = H] was achieved via a multistep synthetic sequence starting from II (R1 = H; R2 = Ac, R4 = H; R6 = C6H5).

IC ICM C07D305-14

CC 30-20 (Terpenes and Terpenoids)

IT 675584-48-2P 675584-49-3P 675584-51-7P **675584-54-0P**

675584-59-5P **675584-61-9P** **675584-63-1P** 675584-65-3P

675584-66-4P 675584-67-5P 675584-68-6P 675584-69-7P 675584-70-0P

675584-71-1P 675584-73-3P 675584-76-6P 675584-77-7P 675584-78-8P

675584-79-9P 675584-80-2P 675584-81-3P 675584-82-4P 675584-83-5P

675584-88-0P 675584-89-1P 675584-90-4P 675584-91-5P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for preparation of taxane derivs. functionalized at the 14-position)

IT **675584-54-0P** **675584-61-9P** **675584-63-1P**

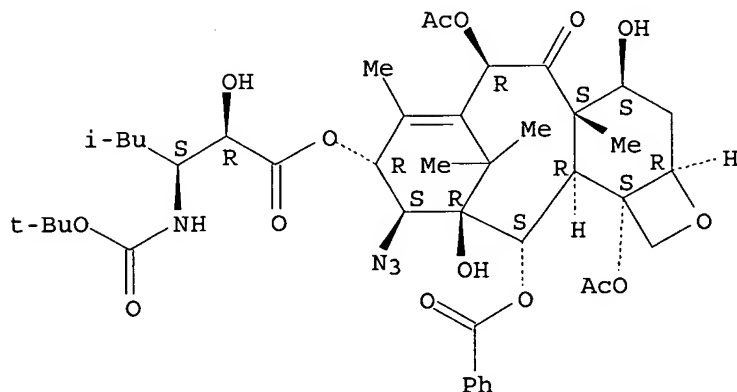
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for preparation of taxane derivs. functionalized at the 14-position)

RN 675584-54-0 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-6,12b-bis(acetyloxy)-10-azido-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 675584-61-9 CAPLUS

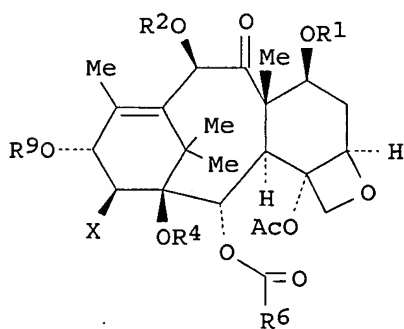
CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-6,12b-bis(acetyloxy)-10-amino-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

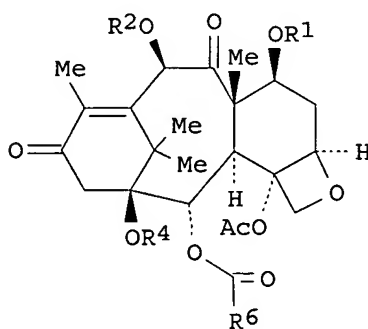
functionalized at the 14-position  
 INVENTOR(S): Fontana, Gabriele; Bombardelli, Ezio; Battaglia, Arturo; Baldelli, Eleonora; Guerrini, Andrea; Gelmi, Maria Luisa; Carenzi, Giacomo; Pocar, Donato  
 PATENT ASSIGNEE(S): Indena S.P.A., Italy  
 SOURCE: PCT Int. Appl., 61 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024706	A2	20040325	WO 2003-EP9866	20030905
WO 2004024706	A3	20040708		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498277	AA	20040325	CA 2003-2498277	20030905
AU 2003267049	A1	20040430	AU 2003-267049	20030905
EP 1537093	A2	20050608	EP 2003-747971	20030905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1681799	A	20051012	CN 2003-821338	20030905
JP 2006503030	T2	20060126	JP 2004-535440	20030905
NO 2005001774	A	20050510	NO 2005-1774	20050411
US 2006122258	A1	20060608	US 2005-527164	20051109
PRIORITY APPLN. INFO.:			IT 2002-MI1921	A 20020910
			WO 2003-EP9866	W 20030905

OTHER SOURCE(S): MARPAT 140:287557  
 GI



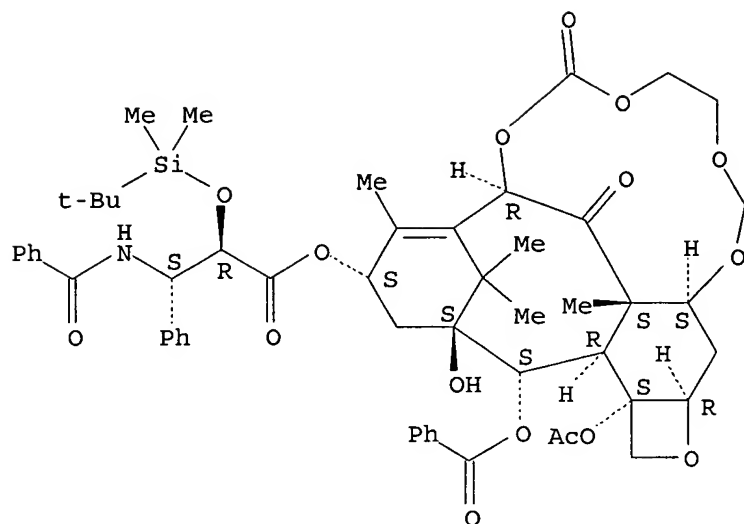
I



II

AB The present invention discloses a general process for the preparation of taxane derivs. such as I [X = N3, NH2, NHR3, :CHR8, OR3; R1 = H, protecting groups; R2 = H, acyl; R3 = alkoxycarbonyl; R3R4 = CO, CS, SO, SO2; R4 = H; R6 = aryl, heteroaryl; R8 = H, alkyl, alkoxycarbonyl; R4R8 = CO; R9 =

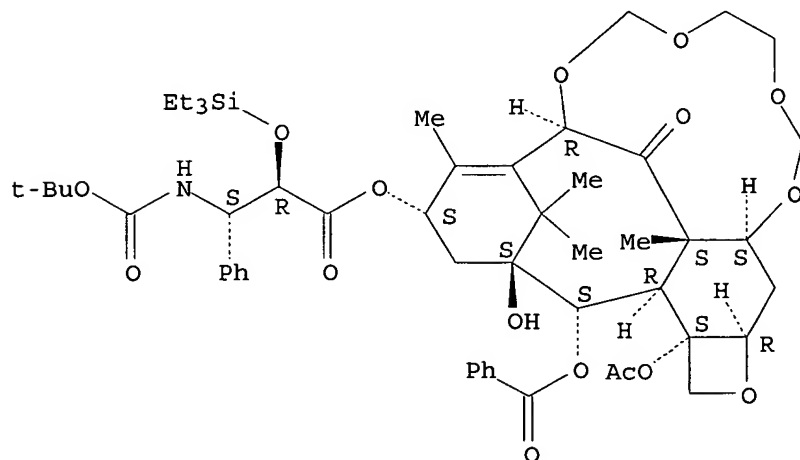
Absolute stereochemistry.



RN 709673-81-4 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -[(triethylsilyl)oxy]-, (9R,10aS,11R,11aS,13aR,14aS,15S,16S,20S)-11a-(acetyloxy)-15-(benzoyloxy)-4,5,9,10,10a,11a,12,13a,14,14a,16,17,20,21-tetradecahydro-16-hydroxy-10a,17,17,19-tetramethyl-10-oxo-9,11-([1,3]benzenomethano)-11H-oxeto[3,2-m]-1,3,6,8-benzotetraoxacyclododecin-20-yl ester, ( $\alpha$ R, $\beta$ S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

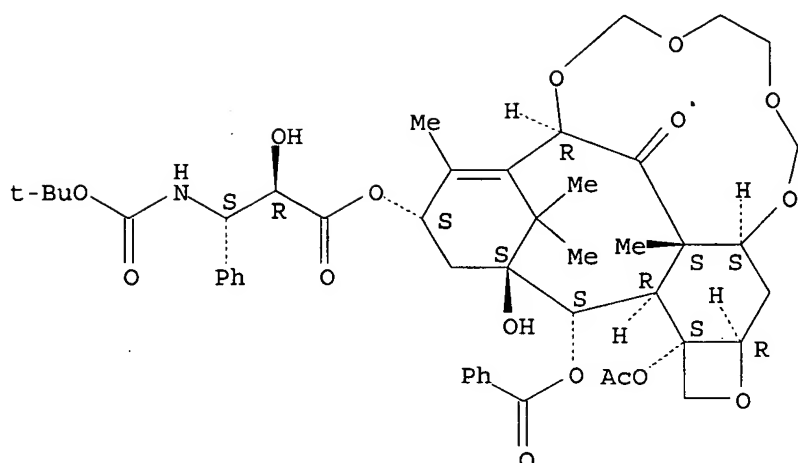
L54 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:252495 CAPLUS

DOCUMENT NUMBER: 140:287557

TITLE: Process for preparation of taxane derivatives





IT 709673-66-5P 709673-78-9P 709673-81-4P

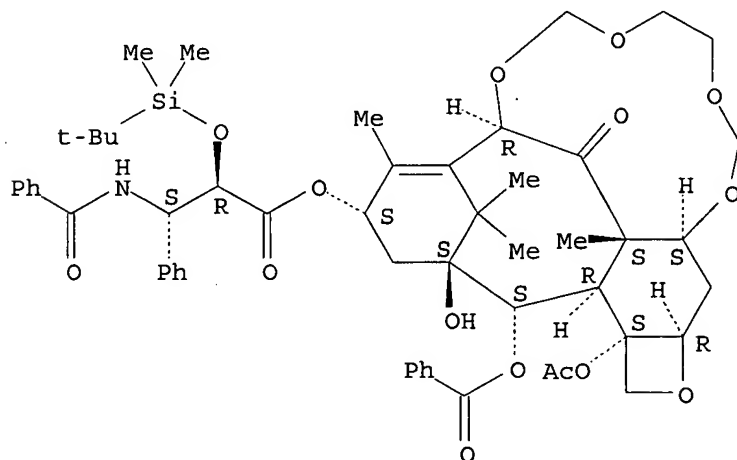
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and biol. activity of macrocyclic taxane analogs)

RN 709673-66-5 CAPLUS

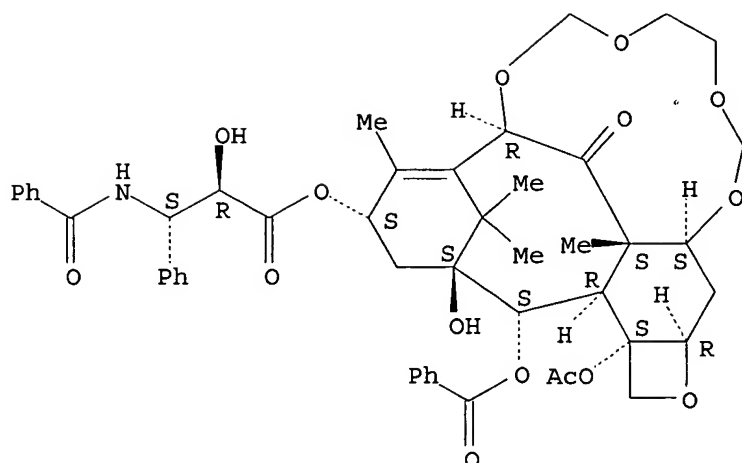
CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (9R,10aS,11R,11aS,13aR,14aS,15S,16S,20S)-11a-(acetyloxy)-15-(benzoyloxy)-4,5,9,10,10a,11a,12,13a,14,14a,16,17,20,21-tetradecahydro-16-hydroxy-10a,17,17,19-tetramethyl-10-oxo-9,11-([1,3]benzenomethano)-11H-oxeto[3,2-m]-1,3,6,8-benzotetraoxacyclododecin-20-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 709673-78-9 CAPLUS

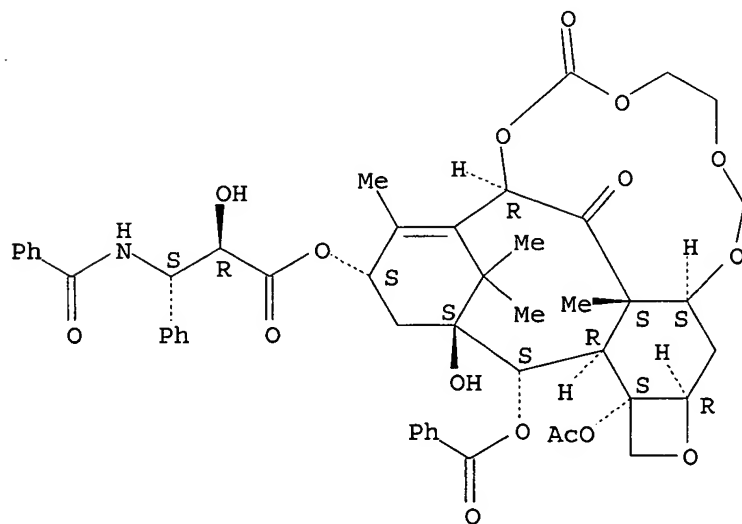
CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (9R,10aS,11R,11aS,13aR,14aS,15S,16S,20S)-11a-(acetyloxy)-15-(benzoyloxy)-4,5,9,10,10a,11a,12,13a,14,14a,16,17,20,21-tetradecahydro-16-hydroxy-10a,17,17,19-tetramethyl-7,10-dioxo-9,11-([1,3]benzenomethano)-11H-oxeto[3,2-m]-1,3,6,8-benzotetraoxacyclododecin-20-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)



RN 709673-73-4 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (9R,10aS,11R,11aS,13aR,14aS,15S,16S,20S)-11a-(acetyloxy)-15-(benzoyloxy)-4,5,9,10,10a,11a,12,13a,14,14a,16,17,20,21-tetradecahydro-16-hydroxy-10a,17,17,19-tetramethyl-10-dioxo-9,11-([1,3]benzenomethano)-11H-oxeto[3,2-m]-1,3,6,8-benzotetraoxacyclododecin-20-yl ester, ( $\alpha$ R, $\beta$ S) - (9CI) (CA INDEX NAME)

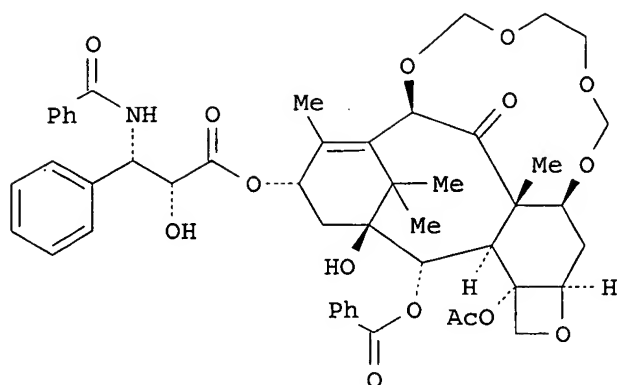
Absolute stereochemistry.



RN 709673-76-7 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (9R,10aS,11R,11aS,13aR,14aS,15S,16S,20S)-11a-(acetyloxy)-15-(benzoyloxy)-4,5,9,10,10a,11a,12,13a,14,14a,16,17,20,21-tetradecahydro-16-hydroxy-10a,17,17,19-tetramethyl-10-oxo-9,11-([1,3]benzenomethano)-11H-oxeto[3,2-m]-1,3,6,8-benzotetraoxacyclododecin-20-yl ester, ( $\alpha$ R, $\beta$ S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



I

AB A series of paclitaxel analogs, e.g. I, possessing a macrocyclic structure between the 7 and 10 positions has been prepared. These compounds possess in vitro activity against a paclitaxel resistant cell line and have in vivo activity comparable to paclitaxel.

CC 30-20 (Terpenes and Terpenoids)

Section cross-reference(s): 1

IT 709673-71-2P 709673-73-4P 709673-76-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and biol. activity of macrocyclic taxane analogs)

IT 114655-02-6P 162375-26-0P 709673-63-2P 709673-66-5P

709673-69-8P 709673-74-5P 709673-75-6P 709673-78-9P

709673-79-0P 709673-80-3P 709673-81-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and biol. activity of macrocyclic taxane analogs)

IT 709673-71-2P 709673-73-4P 709673-76-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and biol. activity of macrocyclic taxane analogs)

RN 709673-71-2 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (9R,10aS,11R,11aS,13aR,14aS,15S,16S,20S)-11a-(acetyloxy)-15-(benzoyloxy)-4,5,9,10,10a,11a,12,13a,14,14a,16,17,20,21-tetradecahydro-16-hydroxy-10a,17,17,19-tetramethyl-10-oxo-9,11-([1,3]benzenomethano)-11H-oxeto[3,2-m]-1,3,6,8-benzotetraoxacyclododecin-20-yl ester, ( $\alpha$ R, $\beta$ S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

794517-81-0 794517-82-1 794517-83-2 794517-84-3 794517-85-4  
 794517-87-6 794517-88-7 794517-90-1 **794517-91-2**  
 794517-92-3 794517-93-4 794517-94-5 794517-95-6 794517-96-7  
 794517-97-8 794517-98-9 795297-26-6, AG 1132 795297-28-8  
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (incorporating protein flexibility in structure-based drug discovery  
 using HIV-1 protease as a test case)

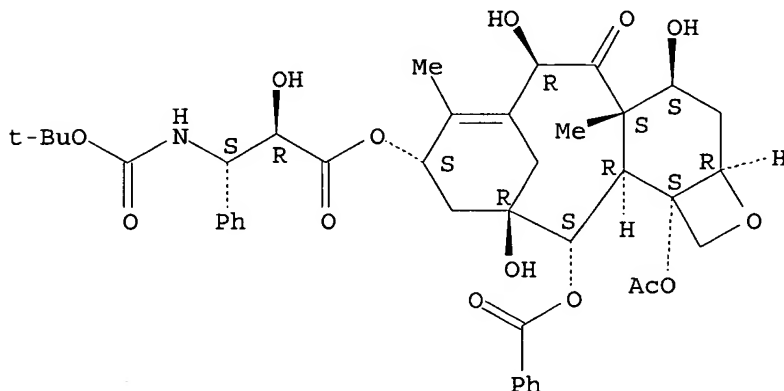
IT **794517-91-2**

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (incorporating protein flexibility in structure-based drug discovery  
 using HIV-1 protease as a test case)

RN 794517-91-2 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonylamino]-  
 $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-  
 (benzyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-  
 trihydroxy-4a,8-dimethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-  
 b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:346260 CAPLUS

DOCUMENT NUMBER: 141:71731

TITLE: Synthesis and biological activity of macrocyclic  
 taxane analogues

AUTHOR(S): Tarrant, James G.; Cook, Donald; Fairchild, Craig;  
 Kadow, John F.; Long, Byron H.; Rose, William C.;  
 Vyas, Dolatrai

CORPORATE SOURCE: Discovery Chemistry, Bristol-Myers Squibb  
 Pharmaceutical Research Institute, Wallingford, CT,  
 06492-7660, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004),  
 14(10), 2555-2558

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:71731

GI

AUTHOR(S): Meagher, Kristin L.; Carlson, Heather A.  
CORPORATE SOURCE: College of Pharmacy, Department of Medicinal  
Chemistry, University of Michigan, Ann Arbor, MI,  
48109-1065, USA  
SOURCE: Journal of the American Chemical Society (2004),  
126(41), 13276-13281  
CODEN: JACSAT; ISSN: 0002-7863  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB We have developed a receptor-based pharmacophore method which utilizes a collection of protein structures to account for inherent protein flexibility in structure-based drug design. Several procedures were systematically evaluated to derive the most general protocol for using multiple protein structures. Most notably, incorporating more protein flexibility improved the performance of the method. The pharmacophore models successfully discriminate known inhibitors from drug-like non-inhibitors. Furthermore, the models correctly identify the bound conformations of some ligands. We used unliganded HIV-1 protease to develop and validate this method. Drug design is always initiated with a protein-ligand structure, and such success with unbound protein structures is remarkable - particularly in the case of HIV-1 protease, which has a large conformational change upon binding. This technique holds the promise of successful computer-based drug design before bound crystal structures are even discovered, which can mean a jump-start of 1-3 yr in tackling some medically relevant systems with computational methods.

CC 1-3 (Pharmacology)

IT 54-62-6 81-11-8 436-05-5, MCMC 10271 865-04-3 865-21-4,  
Vinblastine 1404-15-5 1461-15-0 1947-37-1, 4-7-Cholecystokinin-7  
(swine) 2667-89-2 3785-44-2 6377-18-0 6998-60-3, Rifamycin  
7488-76-8 10236-47-2 11076-29-2 15599-51-6, MCMC 2885 15964-31-5  
22112-79-4 23412-26-2 29883-15-6 30658-43-6 31770-79-3, MCMC 3588  
33605-67-3 34941-71-4 36980-34-4 38716-28-8, MCMC 6171 41600-33-3  
49620-13-5 52196-22-2 54083-22-6, MCMC 4222 54138-84-0 56079-81-3  
58761-87-8 66211-92-5, MCMC 4777 69414-41-1 69558-55-0 69866-21-3,  
MCMC 10279 70774-25-3 72559-06-9 78995-72-9 80394-65-6, MCMC 10434  
84412-94-2 84799-23-5 85807-48-3 88391-91-7, MCMC 7748 93205-34-6  
94168-98-6, MCMC 10469 97068-30-9 97275-40-6 103177-37-3  
103336-05-6, MCMC 6317 108852-90-0 110417-88-4 110816-79-0  
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127779-20-8, Saquinavir 129467-45-4 129981-36-8 136679-36-2  
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573987-39-0 714192-77-5 760215-78-9 794517-69-4 794517-70-7  
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794517-76-3 794517-77-4 794517-78-5 794517-79-6 794517-80-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

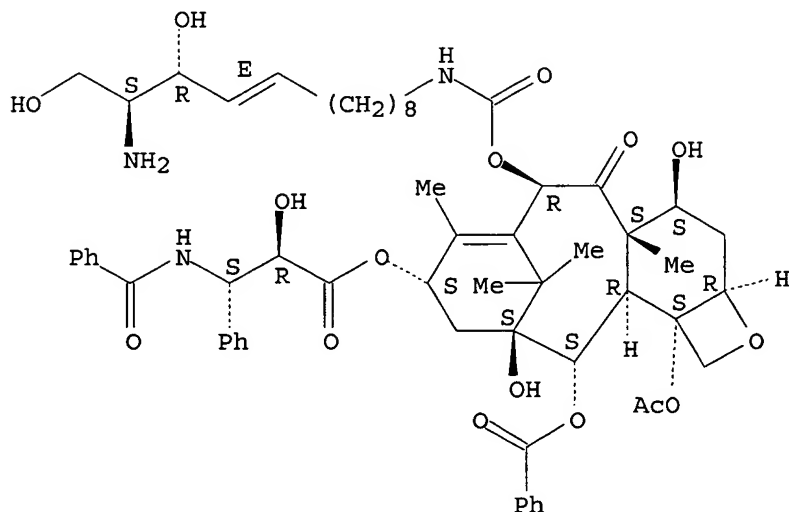
(increasing drug efficiency using conjugates containing drug moiety and linker and substrate for protein or lipid kinase)

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(increasing drug efficiency using conjugates containing drug moiety and linker and substrate for protein or lipid kinase)

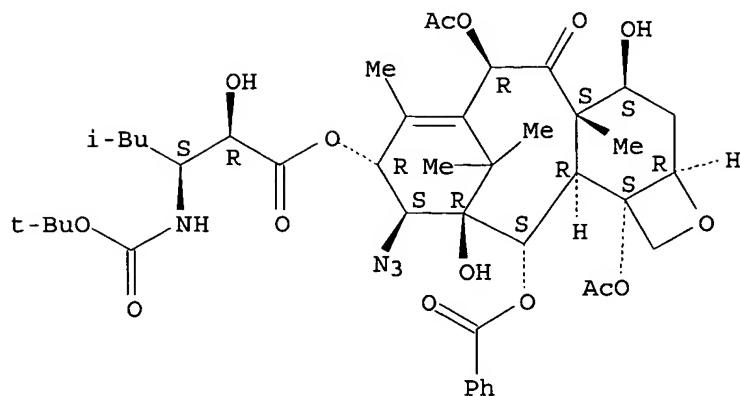
CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-6-[[[(9E,11R,12S)-12-  
amino-11,13-dihydroxy-9-tridecenyl]amino]carbonyl]oxy]-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, (aR,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



TITLE: Incorporating Protein Flexibility in Structure-Based Drug Discovery: Using HIV-1 Protease as a Test Case

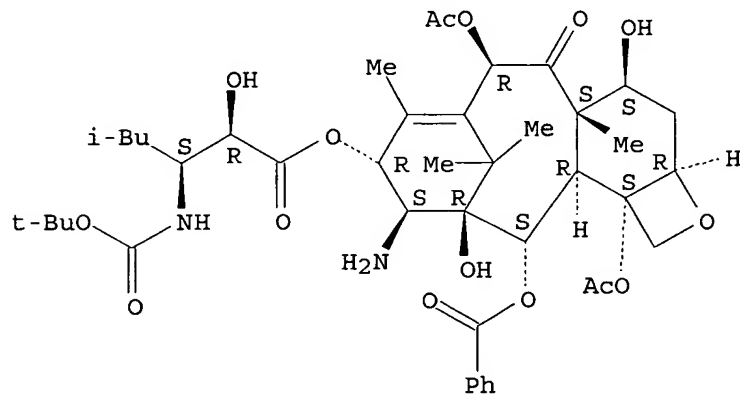
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005035003	A2	20050421	WO 2004-US31148	20040922
WO 2005035003	A3	20050818		
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005148534	A1	20050707	US 2004-948364	20040922
US 2005187147	A1	20050825	US 2004-948707	20040922
PRIORITY APPLN. INFO.:			US 2003-505325P	P 20030922
			US 2004-568340P	P 20040504
			US 2004-581835P	P 20040622
			US 2003-505033P	P 20030922
OTHER SOURCE(S): MARPAT 142:404292				
AB In one embodiment, provided herein are compns. and methods for increasing drug efficiency. In certain embodiments, the compns. contain conjugates having the formula: D-L-S wherein D is a drug moiety; L, which may or may not be present, is a non-releasing linker moiety; and S is a substrate for a protein or lipid kinase that is overexpressed, overactive or exhibits undesired activity in a target system.				
IC ICM A61K047-48				
ICS C07K007-06; A61K038-08; A61P029-00; A61P035-00; A61K031-337; A61K031-475; A61K031-704				
CC 1-12 (Pharmacology)				
Section cross-reference(s): 34, 63				
IT 50-07-7D, Mitomycin C, conjugates 50-18-0D, Cyclophosphamide, conjugates 50-44-2D, 6-Mercaptopurine, conjugates 51-21-8D, 5-Fluorouracil, conjugates 54-62-6D, Aminopterin, conjugates 57-22-7D, Vincristine, conjugates 59-05-2D, Methotrexate, conjugates 91-18-9D, Pteridine, derivs., conjugates 147-94-4D, Cytosine arabinoside, conjugates 148-82-3D, Melphalan, conjugates 518-28-5D, Podophyllotoxin, derivs., conjugates 528-74-5D, Dichloromethotrexate, conjugates 801-52-5D, Porfiromycin, conjugates 865-21-4, Vinblastine 1404-00-8D, Mitomycin, derivs., conjugates 2410-93-7D, Methopterin, conjugates 2998-57-4D, Estramustine, conjugates 3352-69-0D, 4-Desacetylvinblastine, conjugates 11056-06-7D, Bleomycin, derivs., conjugates 15228-71-4D, Leurosidine, conjugates 15663-27-1D, Cisplatin, conjugates 20830-81-3D, Daunorubicin, conjugates 23214-92-8D, Doxorubicin, derivs. 33069-62-4D, Paclitaxel, derivs. 33419-42-0D, Etoposide, conjugates 50935-04-1D, conjugates 53643-48-4D, Vindesine, conjugates 57103-68-1D, Maytansinol, conjugates 78432-77-6, 10-Desacetyl taxol 82855-09-2D, Combretastatin, conjugates 111372-15-7 114977-28-5D, Docetaxel, conjugates 117091-64-2D, Etoposide phosphate, conjugates 146307-39-3 152044-53-6D, Epothilone A, conjugates 152044-54-7D, Epothilone B, conjugates 220167-86-2 849206-51-5 849206-90-2 849206-91-3 849206-92-4 849206-93-5 849206-94-6 850497-99-3 850498-05-4 850498-07-6 850498-09-8 850498-11-2 850498-13-4 850498-15-6 850498-17-8 850498-19-0 850498-21-4 850498-27-0 850498-30-5 850498-33-8 850498-35-0 850498-37-2 850498-39-4 850498-41-8 850498-49-6 850498-51-0 850498-53-2 850498-55-4 850498-57-6 850498-59-8 850498-61-2 850498-63-4 850498-65-6 850498-67-8 850498-69-0 850498-71-4 850498-73-6 850498-76-9				



RN 675584-61-9 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-6,12b-bis(acetyloxy)-10-amino-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:346897 CAPLUS

DOCUMENT NUMBER: 142:404292

TITLE: Compositions and methods for increasing drug efficiency

INVENTOR(S): Ballatore, Carlo; Castellino, Angelo John; Desharnais, Joel; Guo, Zijan; Li, Qing; Newman, Michael James; Sun, Chengzao

PATENT ASSIGNEE(S): Dihedron Corporation, USA

SOURCE: PCT Int. Appl., 404 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

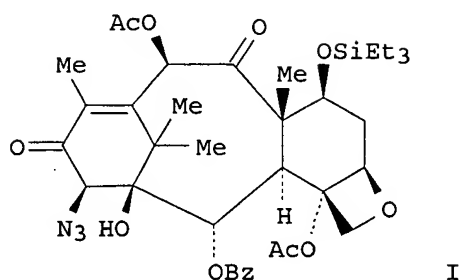
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:



SOURCE: "I.S.O.F.", Bologna, 40129, Italy  
 Tetrahedron (2005), 61(32), 7727-7745  
 CODEN: TETRAB; ISSN: 0040-4020  
 PUBLISHER: Elsevier B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 143:248531  
 GI



AB The base induced deprotonation of H-14 of 7-triethylsilyl- (7-TES-) and 7-tert-butoxycarbonyl- (7-BOC-) protected 13-oxo-baccatins gave the corresponding enolates, which were selectively aminated with electrophilic nitrogen donors, such as azodicarboxylates and tosyl azide. In particular, tosyl azide gave the corresponding 7-BOC- and 7-TES-13-oxo-14β-azido-baccatin III. Alternatively, the last compound was prepared via NaN<sub>3</sub> induced azidation of the 13-silyl enol ether of 7-TES-13-oxo-baccatin III under oxidative (cerium ammonium nitrate) conditions. The 13-silyl enol ether was obtained in a multistep process by DBU induced silylation of 7-TES-13-oxo-baccatin III. 7-TES-13-oxo-14β-azido-baccatin III (I) was used as a key intermediate for the synthesis of a new family of antitumor taxanes containing amino based functional groups at the C-14 position, such as: 14β-azido, 14β-amino, 14β-amino 1,14-carbamate, 14β-amino 1,14-thiocarbamate, and 14β-amino N-tert-butoxycarbonyl-1,14-carbamate.

CC 30-20 (Terpenes and Terpenoids)

IT 675584-48-2P 675584-49-3P 675584-51-7P 675584-54-0P  
 675584-59-5P 675584-61-9P 675584-65-3P 863489-80-9P  
 863489-81-0P 863489-82-1P 863489-83-2P 863489-84-3P 863489-87-6P  
 863489-88-7P 863489-90-1P 863489-91-2P 863489-93-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (selective synthesis of 14β-amino taxanes via stereoselective azidation)

IT 675584-54-0P 675584-61-9P

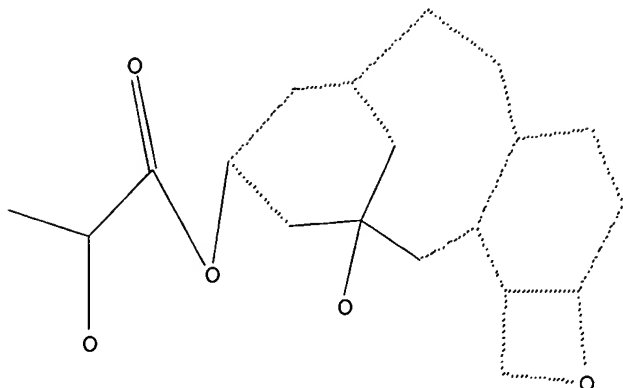
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (selective synthesis of 14β-amino taxanes via stereoselective azidation)

RN 675584-54-0 CAPLUS

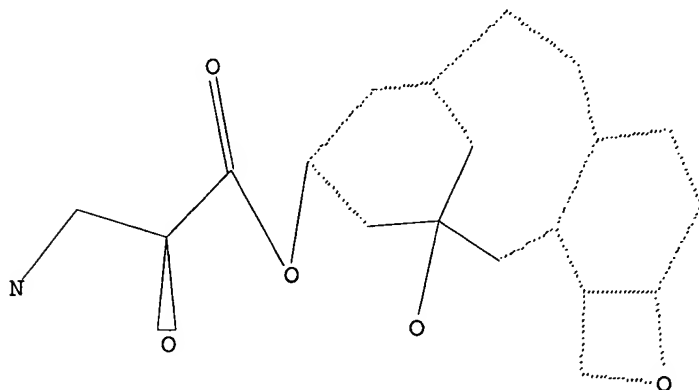
CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy) carbonyl] amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-6,12b-bis(acetyloxy)-10-azido-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

=> d stat que L54  
L3 STR



Structure attributes must be viewed using STN Express query preparation.  
L5 7665 SEA FILE=REGISTRY SSS FUL L3  
L20 STR



Structure attributes must be viewed using STN Express query preparation.  
L22 111 SEA FILE=REGISTRY SUB=L5 SSS FUL L20  
L24 59 SEA FILE=CAPLUS ABB=ON PLU=ON L22  
L44 51 SEA FILE=REGISTRY ABB=ON PLU=ON 11R AND L5  
L45 14 SEA FILE=CAPLUS ABB=ON PLU=ON L44  
L52 1 SEA FILE=CAPLUS ABB=ON PLU=ON L45 AND L24  
L54 13 SEA FILE=CAPLUS ABB=ON PLU=ON L45 NOT L52

=> d ibib abs hitind hitstr L54 1-13

L54 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2005:589047 CAPLUS  
DOCUMENT NUMBER: 143:248531  
TITLE: Selective synthesis of 14 $\beta$ -amino taxanes  
AUTHOR(S): Battaglia, Arturo; Baldelli, Eleonora; Bombardelli,  
Ezio; Carenzi, Giacomo; Fontana, Gabriele; Gelmi,  
Maria Luisa; Guerrini, Andrea; Pocar, Donato  
CORPORATE SOURCE: Istituto CNR per la Sintesi Organica e Fotoreattività

## STRUCTURE SEARCH #3

=> file registry

FILE 'REGISTRY' ENTERED AT 13:52:04 ON 19 SEP 2006

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DICTIONARY FILE UPDATES: 18 SEP 2006 HIGHEST RN 907539-37-1

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<http://www.cas.org/ONLINE/UG/regprops.html>

=> file caplus

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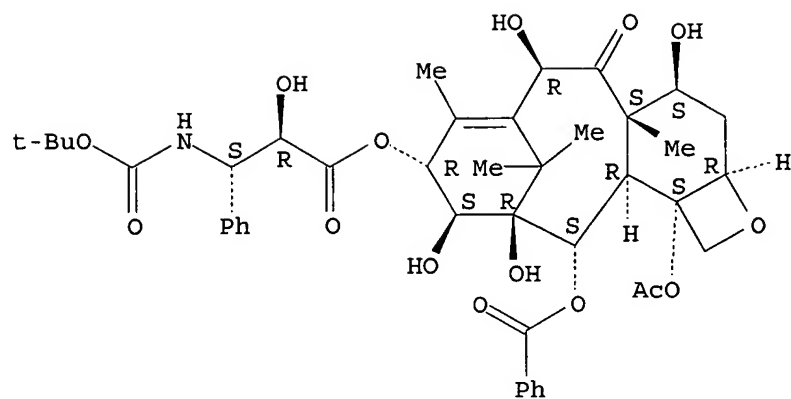
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=> s L45 not L52

L54

13 L45 NOT L52

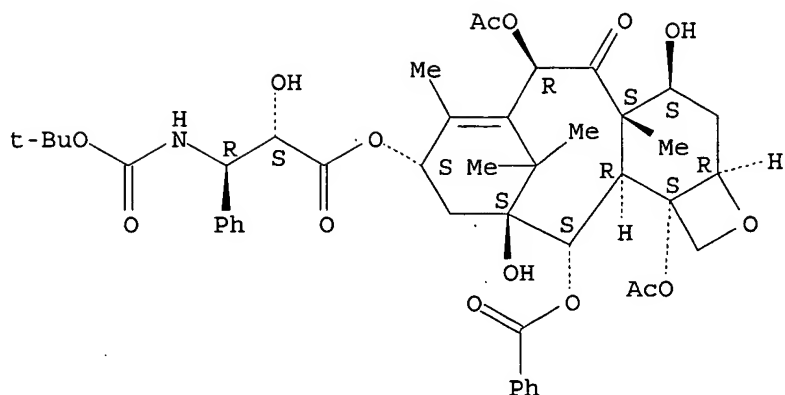
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REFERENCE COUNT:

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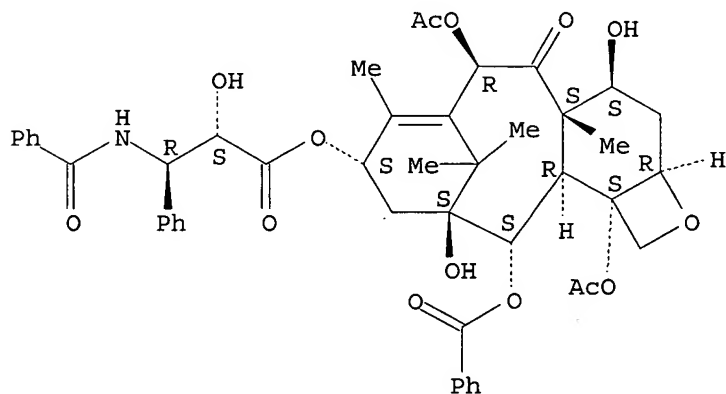
THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



RN 149197-23-9 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 159143-50-7 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9R,10S,11R,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,10,11-tetrahydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ R, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

cross-validation  $r^2_{cv}$  of 0.640 and conventional  $r^2$  of 0.868. The predictive ability of training set model was tested on the test set of 14 compds. The tests not only revealed the robustness of the CoMFA model but demonstrated that for this model  $r^2_{pred}$  based on the mean activity of test set compds. can accurately estimate external predictivity but  $r^2_{pred}$  based on the mean activity of training set compds. overestimated the model. The CoMFA model explained why the activity of taxoid is sensitive to the stereochem. of the atoms at C-2' and C-3' positions and the presence of hydroxyl group at C-2' position. The other factors affecting activity were also elucidated according to standard coefficient contour maps of steric

and

electrostatic fields derived from the CoMFA model.

CC 1-3 (Pharmacology)

Section cross-reference(s): 22, 26

IT 33069-62-4 33069-62-4D, Paclitaxel, analogs 95603-46-6 110259-00-2  
 114977-28-5 114977-28-5D, Taxotere, analogs 114977-30-9 114977-31-0  
 125257-07-0 125354-16-7 **125354-17-8** 125354-18-9  
 125354-19-0 125355-66-0 132160-32-8 133524-66-0 133524-67-1  
 133524-70-6 133577-30-7 133577-36-3 143842-96-0 143842-97-1  
 146384-06-7 146384-07-8 146384-09-0 148548-12-3 148548-19-0  
 148548-20-3 148548-28-1 149107-89-1 **149197-23-9**  
 155399-29-4 155399-30-7 155399-31-8 157187-76-3 157956-84-8  
 158307-77-8 158810-91-4 159143-49-4 **159143-50-7**  
 160161-54-6 160161-55-7 160161-58-0 160161-59-1 160238-30-2  
 160238-31-3 160238-37-9 160238-39-1 160313-74-6 160334-85-0  
 160582-72-9 160747-47-7 160747-74-0 160747-84-2 165268-02-0  
 165268-03-1 165268-09-7 165268-10-0 170241-03-9 170241-04-0  
 172481-73-1 172481-74-2 172481-75-3 172481-76-4 172481-79-7  
 172481-80-0 172481-83-3 172481-84-4 173101-48-9 189136-30-9  
 195194-48-0 195194-52-6 199657-56-2 199657-57-3 199657-58-4  
 199657-61-9 199657-62-0 199657-63-1 199657-64-2 199657-65-3  
 199657-66-4 199657-67-5 199657-68-6 199657-69-7 199657-70-0  
 199657-71-1 199657-72-2 199657-73-3 199657-74-4 199657-75-5  
 199657-76-6 199737-26-3 199737-27-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(comparative mol. field anal. of paclitaxel analogs)

IT **125354-17-8 149197-23-9 159143-50-7**

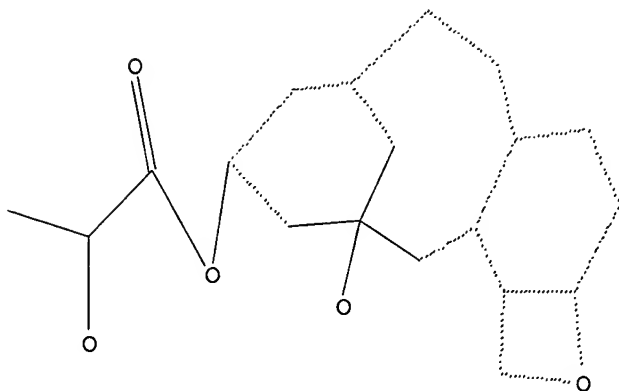
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(comparative mol. field anal. of paclitaxel analogs)

RN 125354-17-8 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Structure attributes must be viewed using STN Express query preparation.

L5 7665 SEA FILE=REGISTRY SSS FUL L3  
 L44 51 SEA FILE=REGISTRY ABB=ON PLU=ON 11R AND L5  
 L45 14 SEA FILE=CAPLUS ABB=ON PLU=ON L44

=> s L45 and L24  
 L52 1 L45 AND L24

=> s L45 and L24 and L49  
 L53 0 L45 AND L24 AND L49

=> d ibib abs hitind hitstr L52 1

L52 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:31653 CAPLUS

DOCUMENT NUMBER: 128:30043

TITLE: Comparative Molecular Field Analysis of A Series of  
 Paclitaxel Analogs

AUTHOR(S): Zhu, Qiqing; Guo, Zongru; Huang, Niu; Wang, Minmin;  
 Chu, Fengming

CORPORATE SOURCE: Department of Synthetic Medicinal Chemistry Institute  
 of Materia Medica Chinese Academy of Medical Sciences,  
 Peking Union Medical College, Beijing, 100050, Peop.  
 Rep. China

SOURCE: Journal of Medicinal Chemistry (1997), 40(26),  
 4319-4328

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

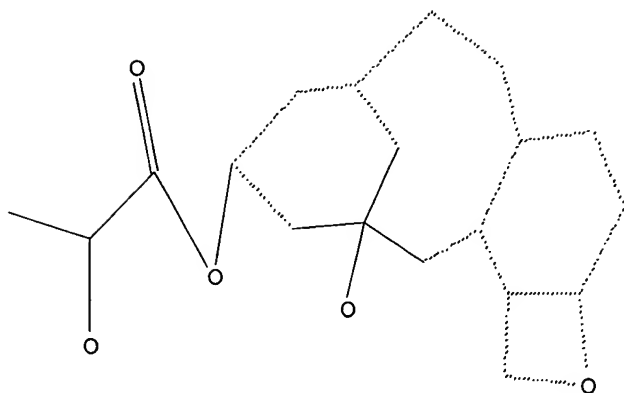
DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of 94 paclitaxel analogs exhibiting antitumor activity by promoting the assembly of microtubules and inhibiting the disassembly process of microtubules to tubulin were investigated using the comparative mol. field anal. (CoMFA) method. These compds. belonging to 10 structural classes were randomly divided into a training set of 80 compds. and a test set of 14 compds. Since the 3-dimensional structure of ligand-receptor complex is unknown, from x-ray and NMR data, the authors rationally selected the 3-dimensional structure of paclitaxel in a polar solution as the active conformation and starting structure for mol. modeling, the other mols. were aligned using this mol. model as the template. The most optimal CoMFA yielded a 2-component model, with significant

L3

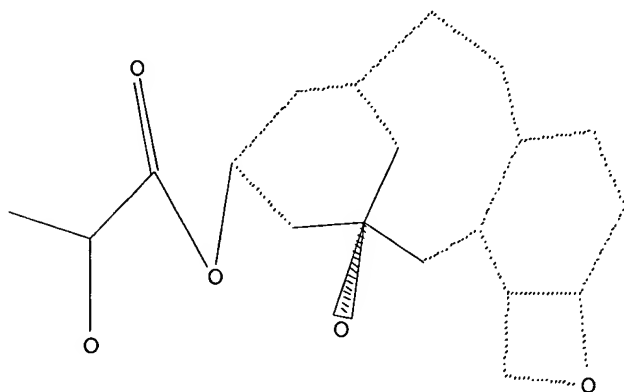
STR



Structure attributes must be viewed using STN Express query preparation.

L5 7665 SEA FILE=REGISTRY SSS FUL L3

L14 STR



Structure attributes must be viewed using STN Express query preparation.

L16 0 SEA FILE=REGISTRY SUB=L5 SSS FUL L14

100.0% PROCESSED 7665 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

=> d stat que L45

L3 STR



=> => ☐ STRUCTURE SEARCH #2

=> file registry

FILE 'REGISTRY' ENTERED AT 13:49:31 ON 19 SEP 2006

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FILE LAST UPDATED: 18 Sep 2006 (20060918/ED)

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<http://www.cas.org/infopolicy.html>

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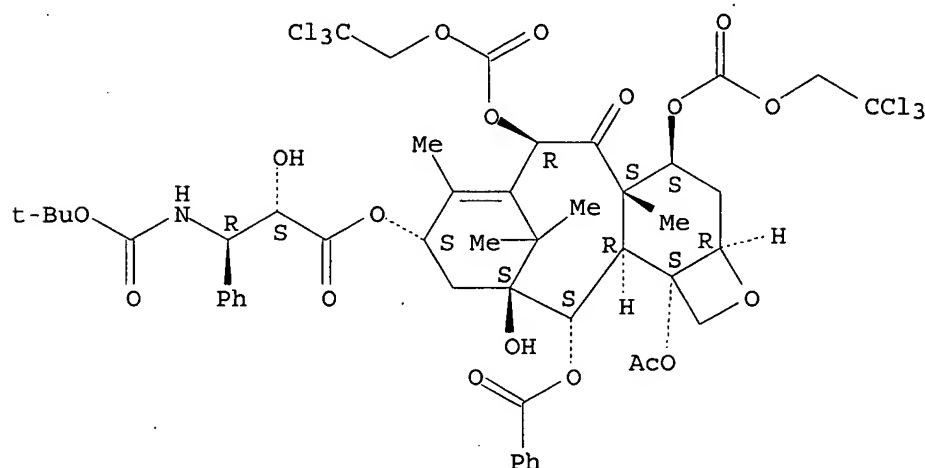
=> d stat que L16



RN 114977-25-2 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4,6-bis[[[(2,2,2-trichloroethoxy)carbonyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



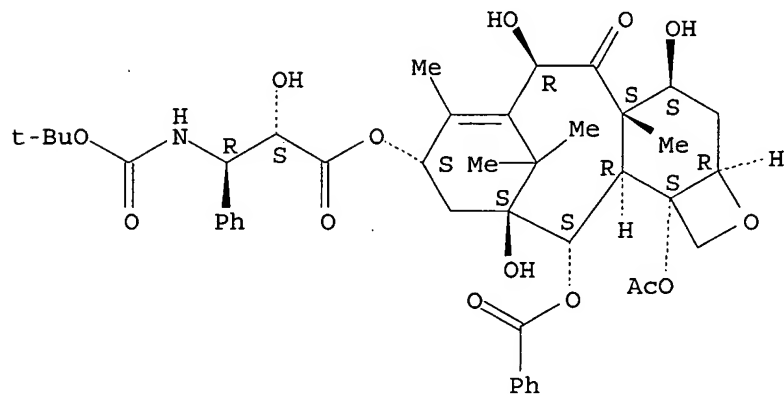
IT 114977-29-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation of, as antitumor agent)

RN 114977-29-6 CAPLUS

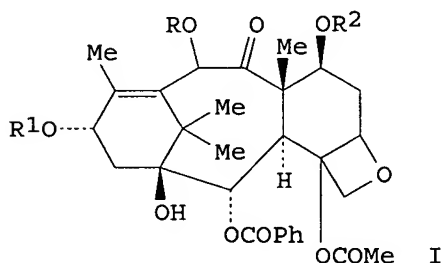
CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



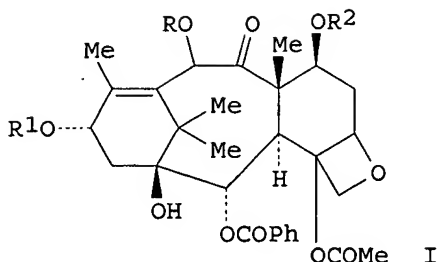
DOCUMENT NUMBER: 109:22762  
 TITLE: Preparation of taxol derivatives as antitumor agents  
 INVENTOR(S): Colin, Michel; Guenard, Daniel; Gueritte-Voegelein, Françoise; Potier, Pierre  
 PATENT ASSIGNEE(S): Rhone-Poulenc Sante, Fr.  
 SOURCE: Eur. Pat. Appl., 12 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 253738	A1	19880120	EP 1987-401668	19870716
EP 253738	B1	19900131		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2601675	A1	19880122	FR 1986-10400	19860717
FR 2601675	B1	19880923		
US 4814470	A	19890321	US 1987-73156	19870714
AU 8775677	A1	19880121	AU 1987-75677	19870715
AU 591309	B2	19891130		
ZA 8705179	A	19880330	ZA 1987-5179	19870715
JP 63030479	A2	19880209	JP 1987-176071	19870716
JP 06051689	B4	19940706		
AT 49962	E	19900215	AT 1987-401668	19870716
CA 1278304	A1	19901227	CA 1987-542299	19870716
PRIORITY APPLN. INFO.:			FR 1986-10400	A 19860717
			EP 1987-401668	A 19870716
OTHER SOURCE(S):	MARPAT 109:22762			
GI				



AB The title compds. (I; R = H, Ac; R1 = PhCHR4CHR3CO; R2 = H; 1 of R3, R4 = OH and the other = NHCO2CMe3) were prepared I (R = R1 = R2 = H) was stirred with ClCO2CH2CCl3 in pyridine to give I (R = R2 = CO2CH2CCl3, R1 = H) which was heated 18 h at 70° with PhCH:CHCO2H in PhMe containing DCC and dimethylaminopyridine to give I (R1 = trans-PhCH:CHCO, R, R2 as above). The latter was added to an MeCN solution of Me3CO2CNClNa (treated with AgNO3) and OsO4 and the mixture stirred 68 h in the dark with addnl. reagent addition to give I [R1 = (2'R,3'S)-COCH(OH)CHPhNHCO2CMe3, R, R2 as above] which was stirred 2 h in HOAc containing Zn to give I [R = R2 = H, R1 = (2'R,3'S)-COCH(OH)CHPhNHCO2CMe3]. At 1-10 mg/kg i.p. I are active in mice inoculated with L1210 or P388 leukemia.

IT 114977-25-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and reaction of, in preparation of antitumor agents)



AB The title compds. [I; R = H, OAc; R1 = (2'R,3'S)-COCH(OH)CHPhNHBz; R2 = H] were prepared as antitumor agents (no data). I (R = R2 = CO2CH2CCl3, R1 = COCH:CHPh) (preparation given) was added to an MeCN solution of Me3CO2CNC1Na (treated with AgNO3) and OsO4 and the mixture stirred 68 h in the dark with addnl. reagent addition to give I [R1 = COCH(OH)CHPhNHCO2CMe3, R, R2 as above] which was stirred at 0° in MeCN with Me3SiI to give I [R1 = COCH(OH)CHPhNH2, R, R2 as above]. The latter were stirred in pyridine with BzCl to give I [R1 = COCH(OH)CHPhNHBz, R, R2 as above] which was stirred 2 h in HOAc containing Zn to give I [R = R2 = H, R1 = COCH(OH)CHPhNHBz].

IT 114977-25-2P

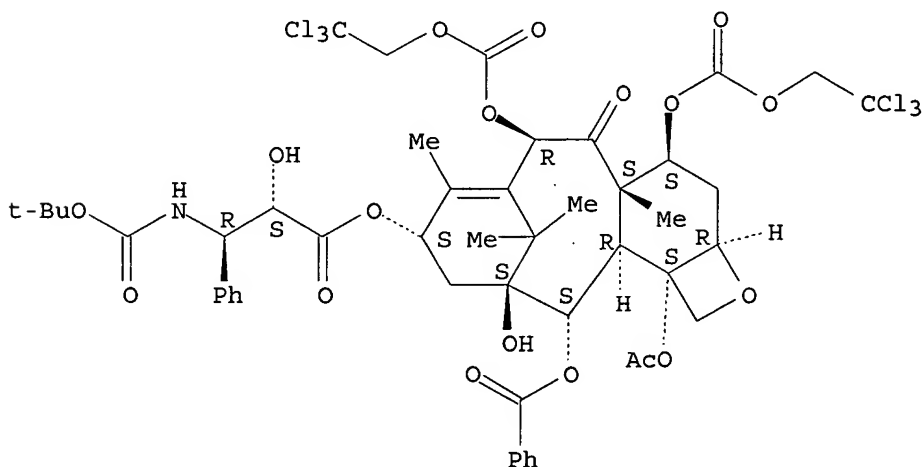
RL: SPN (Synthetic preparation); FORM (Formation, nonpreparative); PREP (Preparation)

(formation of, in preparation of antitumor agents)

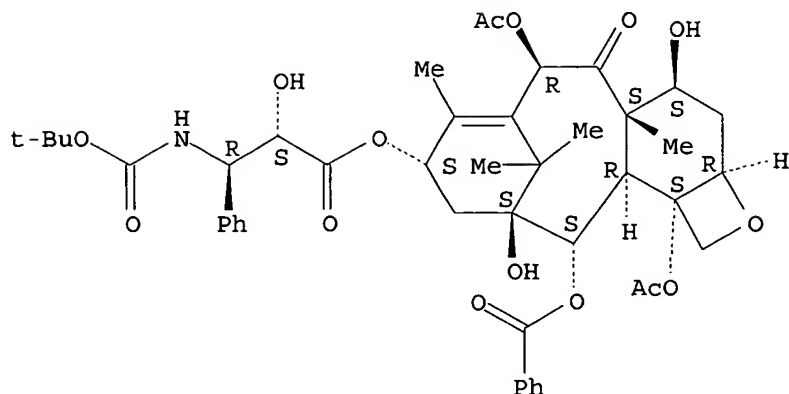
RN 114977-25-2 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-  
 $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-  
 (benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-  
 4a,8,13,13-tetramethyl-5-oxo-4,6-bis[[[(2,2,2-trichloroethoxy)carbonyl]oxy]-  
 7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 52 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1988:422762 CAPLUS

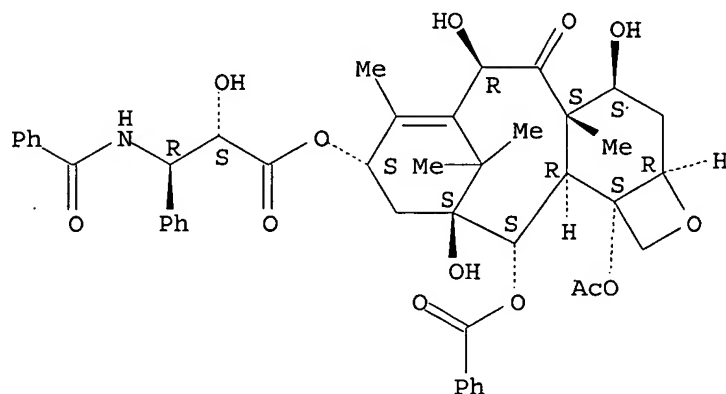


L51 ANSWER 51 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1988:422763 CAPLUS  
 DOCUMENT NUMBER: 109:22763  
 TITLE: Preparation of taxol and of 10-desacetyl-10-taxol as antitumor agents  
 INVENTOR(S): Colin, Michel; Guenard, Daniel; Gueritte-Voegelein, Francoise; Potier, Pierre  
 PATENT ASSIGNEE(S): Rhone-Poulenc Sante, Fr.  
 SOURCE: Eur. Pat. Appl., 8 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 253739	A1	19880120	EP 1987-401669	19870716
EP 253739	B1	19891011		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2601676	A1	19880122	FR 1986-10401	19860717
FR 2601676	B1	19880923		
US 4857653	A	19890815	US 1987-73154	19870714
AU 8775678	A1	19880121	AU 1987-75678	19870715
AU 591310	B2	19891130		
ZA 8705180	A	19880330	ZA 1987-5180	19870715
JP 63030478	A2	19880209	JP 1987-176070	19870716
JP 06004607	B4	19940119		
AT 47137	E	19891015	AT 1987-401669	19870716
CA 1278303	A1	19901227	CA 1987-542297	19870716
PRIORITY APPLN. INFO.:			FR 1986-10401	A 19860717
			EP 1987-401669	A 19870716
OTHER SOURCE(S):			MARPAT 109:22763	
GI				

tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



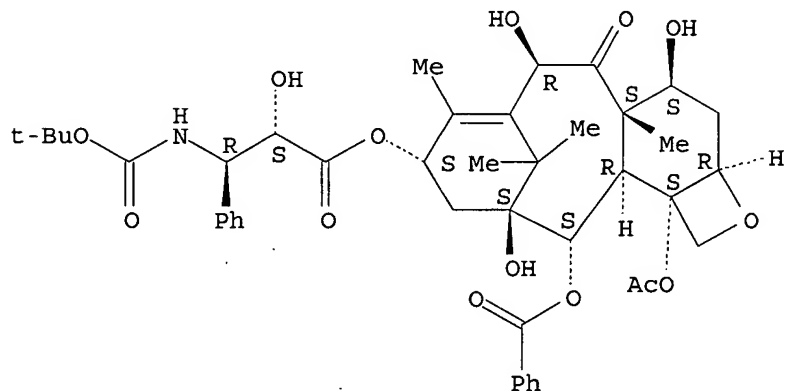
IT 114977-29-6P 125354-17-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as taxol analog)

RN 114977-29-6 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R) - (9CI) (CA INDEX NAME)

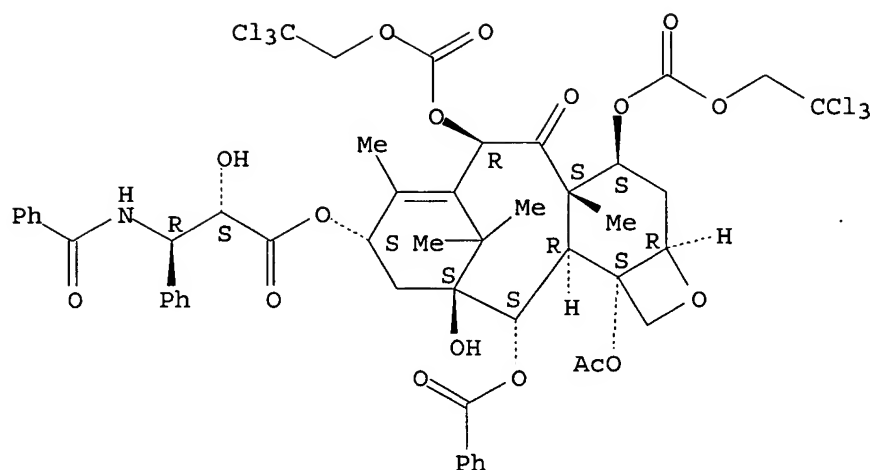
Absolute stereochemistry.



RN 125354-17-8 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



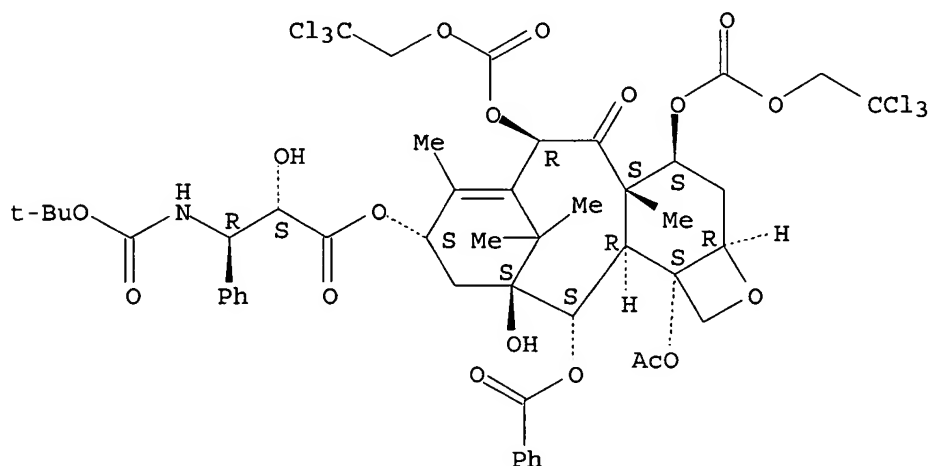
IT 114977-25-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and detrichloroethoxycarbonylation or de-tert-butylloxycarbonylation of)

RN 114977-25-2 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4,6-bis[[2,2,2-trichloroethoxy]carbonyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



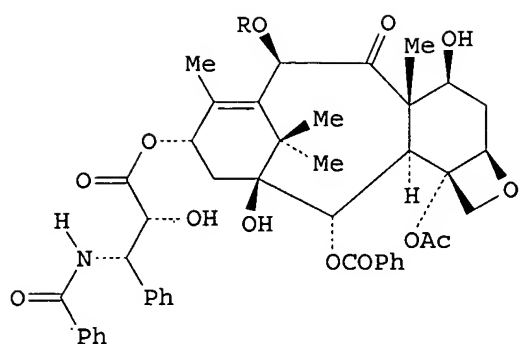
IT 125354-13-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as deacetyltaxol analog)

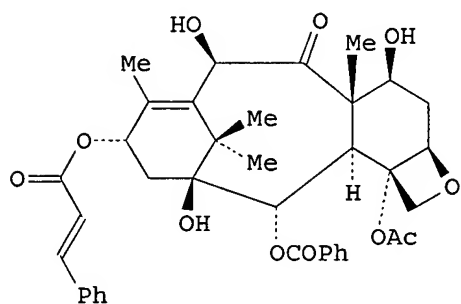
RN 125354-13-4 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-





I



II

AB Taxol (I; R = Ac) 10-deacetyltaxol (I; R = H) and their side chain analogs were obtained via a Sharpless oxyamination reaction on 13-cinnamoylbaccatin III (II). Asym. induction was studied using different bridgehead amines as chiral ligands. This procedure constitutes an alternative route to taxol derivs. for biol. studies.

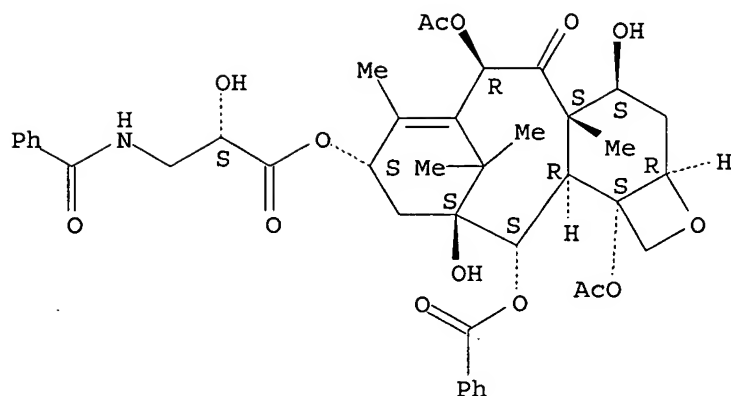
IT 125354-12-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and detrichloroethoxycarbonylation of)

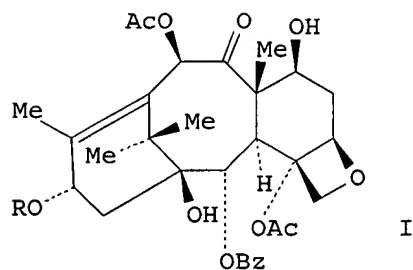
RN 125354-12-3 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-  
dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4,6-bis[[[(2,2,2-  
trichloroethoxy)carbonyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-  
b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ (.alph  
a.S\*, $\beta$ R\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]-(9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 50 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1990:119169 CAPLUS  
DOCUMENT NUMBER: 112:119169  
TITLE: Application of the vicinal hydroxyamination reaction  
with asymmetric induction to the hemisynthesis of  
taxol and analogs  
AUTHOR(S): Mangatal, L.; Adeline, M. T.; Guenard, D.;  
Gueritte-Voegelein, F.; Potier, P.  
CORPORATE SOURCE: Inst. Chim. Subst. Nat., CNRS, Gif-sur-Yvette, 91198,  
Fr.  
SOURCE: Tetrahedron (1989), 45(13), 4177-90  
CODEN: TETRAB; ISSN: 0040-4020  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 112:119169  
GI



AB Taxol (I, R = H) a potent inhibitor of cell replication, enhances the assembly of tubulin into stable microtubules and promotes the formation of microtubule bundles in cells. In addition to its unique mechanism of action, taxol exhibits unusual promise as an antitumor agent, but its application in cancer chemotherapy is hampered by its limited availability. In order to better define the structure-activity profile of taxol or the design of more accessible drugs and to provide insight into the chemical features of the taxol-microtubule interaction, taxol analogs I [R = (R)-, (S)-HOCHMeCO, HOCH(CH<sub>2</sub>Ph)CO, BzNHCH<sub>2</sub>CH(OH)CO] were synthesized from baçcatin III through esterification at the hindered 13-hydroxyl. Although less biol. active than taxol, analogs I [R = (R)-, and (S)-PhCH<sub>2</sub>CH(OH)CO, R-BzNHCH<sub>2</sub>CH(OH)CO] promote the polymerization of tubulin and are cytotoxic; I

[R = PhCH<sub>2</sub>CH(OH)CO] were most effective. Interestingly, tubulin polymerization was sensitive to the C-2' configuration only when the amide substituent was present in the side chain. This observation suggests that the 3'-amide substituent plays an important role in preorganizing the taxol side chain to bind to microtubules.

IT 131896-67-8P

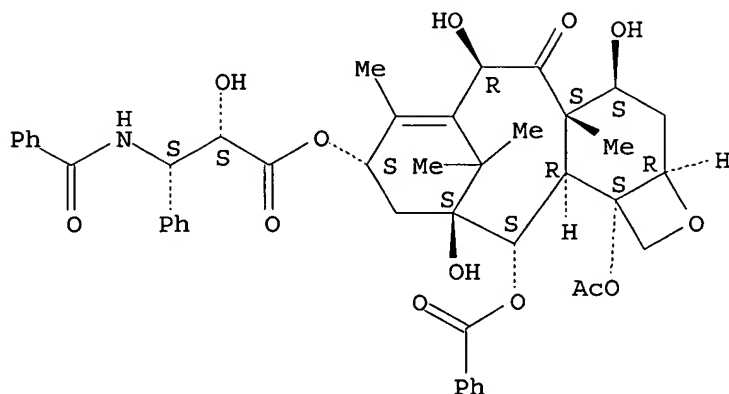
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and tubulin polymerization by)

RN 131896-67-8 CAPLUS

CN Propanoic acid, 3-(benzoylamino)-2-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4β,4aβ,6β,9α(S\*),11.alpha.,12α,12aα,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

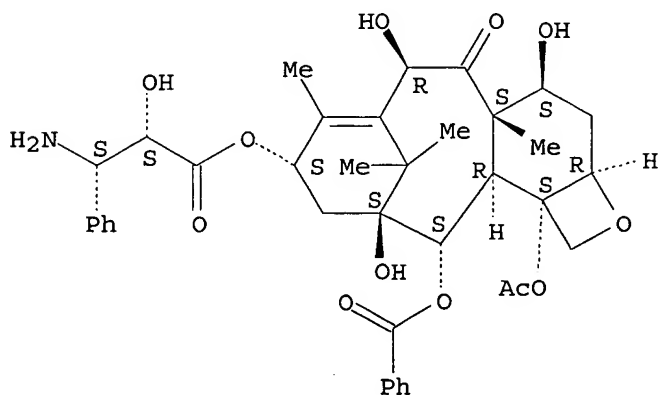
Absolute stereochemistry.



RN 133577-37-4 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -amino- $\alpha$ -hydroxy-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*)],11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L51 ANSWER 49 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:122749 CAPLUS

DOCUMENT NUMBER: 114:122749

TITLE: Biologically active taxol analogs with deleted A-ring side chain substituents and variable C-2' configurations

AUTHOR(S): Swindell, Charles S.; Krauss, Nancy E.; Horwitz, Susan B.; Ringel, Israel

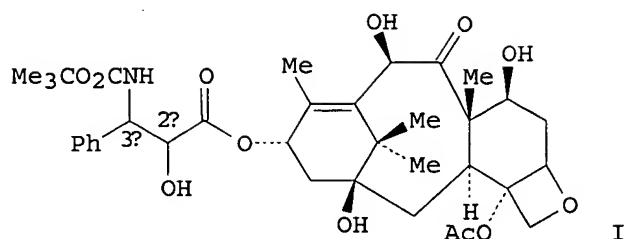
CORPORATE SOURCE: Dep. Chem., Bryn Mawr Coll., Bryn Mawr, PA, 19010, USA

SOURCE: Journal of Medicinal Chemistry (1991), 34(3), 1176-84  
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB A variety of synthetic analogs of taxol, a naturally occurring antitumor diterpene, were examined for their potency to inhibit microtubule disassembly. For some of the compds., the in vitro cytotoxic properties showed a good correlation with the tubulin assay. This structure-activity relationship study confirms that inhibition of microtubule disassembly is quite sensitive to the configuration at C-2' and C-3'. A correlation between the conformation of the side chain at C-13 and the activity is suggested. Of all the compds. examined, one of the most potent in inhibiting microtubule disassembly and in inhibiting murine P388 leukemic cells, N-debenzoyl-N-tert-(butoxycarbonyl)-10-deacetyltaxol, named taxotere [(2'R,3'S)-I], was selected for evaluation as a potential anticancer agent.

IT 133577-33-0P 133577-35-2P 133577-37-4P

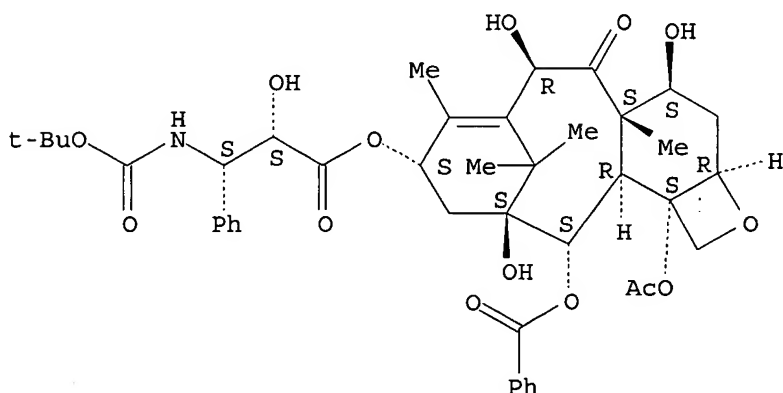
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as inhibitor of microtubule disassembly)

RN 133577-33-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 133577-35-2 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

activity. The importance of the side chain was shown by the much lower activity as compared to taxol of analogs lacking all or part of the side chain. The effect of stereochem. at the C-2' position on fungitoxicity towards oomycetes was similar to that reported previously on mammalian microtubule assembly.

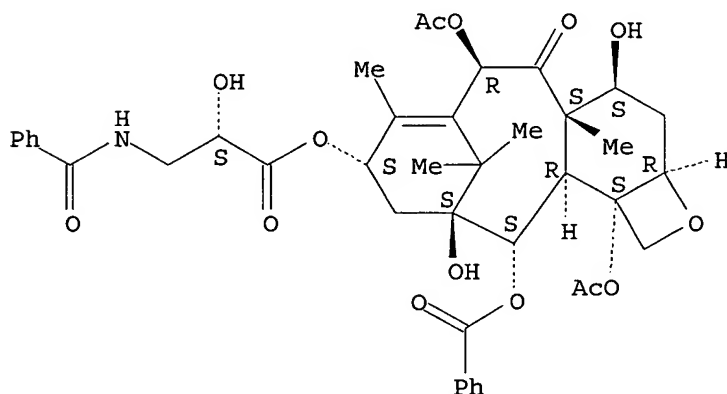
IT 131896-67-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(fungicidal activity of, structure in relation to)

RN 131896-67-8 CAPLUS

CN Propanoic acid, 3-(benzoylamino)-2-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ (S\*),11.alpha.,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 48 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:247557 CAPLUS

DOCUMENT NUMBER: 114:247557

TITLE: Relationships between the structure of taxol analogs and their antimitotic activity

AUTHOR(S): Gueritte-Voegelein, Françoise; Guenard, Daniel; Lavelle, François; Le Goff, Marie Therese; Mangatal, Lydie; Potier, Pierre

CORPORATE SOURCE: Inst. Chim. Subst. Nat., Gif-sur-Yvette, 91198, Fr.

SOURCE: Journal of Medicinal Chemistry (1991), 34(3), 992-8

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

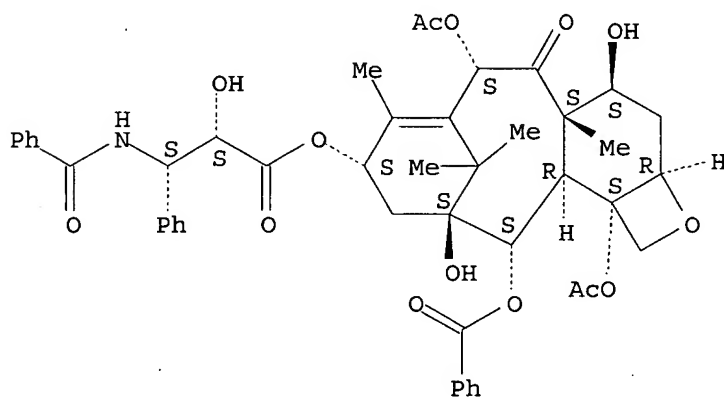
AB Low-toxicity, antitumor compound NSC-LSC1 I, a taxol analog, is manufactured with a callus culture developed from albumens of *Taxus*, especially *Taxus brevifolia*. In vitro antitumor activity of I was shown by its IC<sub>50</sub> against the mouse leukemic cells P388 and human squamous carcinoma cells KB, 3.3 and 19 ng/mL, resp.

IT 147557-12-8P  
 RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)  
 (manufacture of, with callus culture of *Taxus brevifolia*, as antitumor agent)

RN 147557-12-8 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aa,4 $\beta$ ,4a $\beta$ ,6 $\alpha$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*),11.alpha.,12 $\alpha$ ,12aa,12ba]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 47 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:55951 CAPLUS

DOCUMENT NUMBER: 118:55951

TITLE: Antifungal properties of taxol and various analogs

AUTHOR(S): Young, D. H.; Michelotti, E. L.; Swindell, C. S.; Krauss, N. E.

CORPORATE SOURCE: Res. Lab., Rohm and Haas Co., Spring House, PA, 19477, USA

SOURCE: Experientia (1992), 48(9), 882-5  
 CODEN: EXPEAM; ISSN: 0014-4754

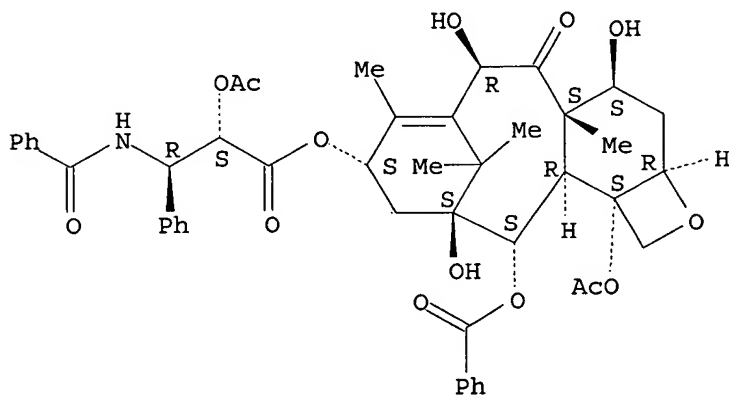
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The antimitotic agent taxol was tested for toxicity towards fungi from different taxonomic groups and found to be particularly active against oomycete fungi. In terminating zoospore cysts of the oomycete *Phytophthora capsici* the mechanism of action of taxol was shown to involve inhibition of mitosis, presumably resulting from an effect on microtubules. Various taxol analogs with deleted A-ring C-13 side chain substituents were tested for toxicity towards *P. capsici* and *Aphanomyces cochlioides* to provide insight into structural features required for

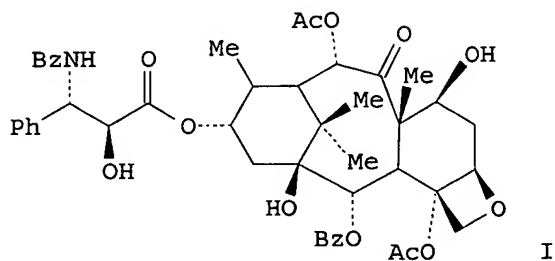
RN 151509-29-4 CAPLUS  
 CN Benzenepropanoic acid,  $\alpha$ -(acetyloxy)- $\beta$ -(benzoylamino)-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*)],11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 46 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1993:232375 CAPLUS  
 DOCUMENT NUMBER: 118:232375  
 TITLE: Antitumor compound NSC-LSC1 and its manufacture with callus culture of Taxus brevifolia  
 INVENTOR(S): Saito, Koji; Ohashi, Hiroaki; Tahara, Makoto; Sakamoto, Tetsuo; Hibi, Masaaki  
 PATENT ASSIGNEE(S): Nippon Steel Corp., Japan  
 SOURCE: PCT Int. Appl., 18 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9302067 A1		19930204	WO 1992-JP917	19920717
W: CA, JP, KR, US				
RW: AT, BE, CH, DE, FR, GB, IT, SE				
PRIORITY APPLN. INFO.: GI			JP 1991-176902	19910717





= OH, R2 = NHCO2CMe3), possess a different conformation with no hydrophobic interactions between the side chain and the taxan skeleton.

IT 114977-29-6 133577-33-0

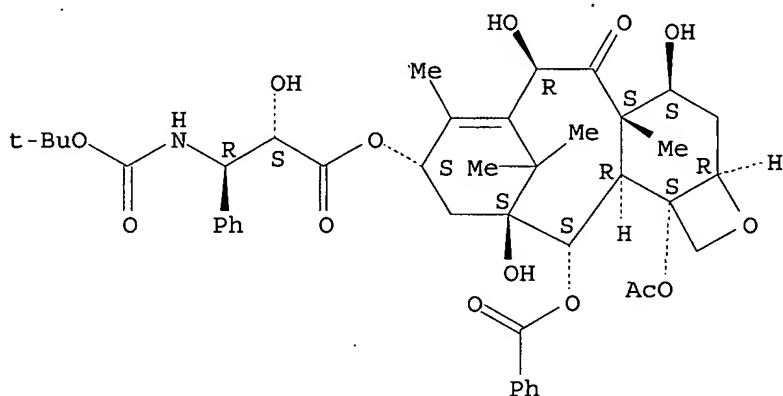
RL: RCT (Reactant); RACT (Reactant or reagent)

(conformation determined by NMR and mol. modeling)

RN 114977-29-6 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

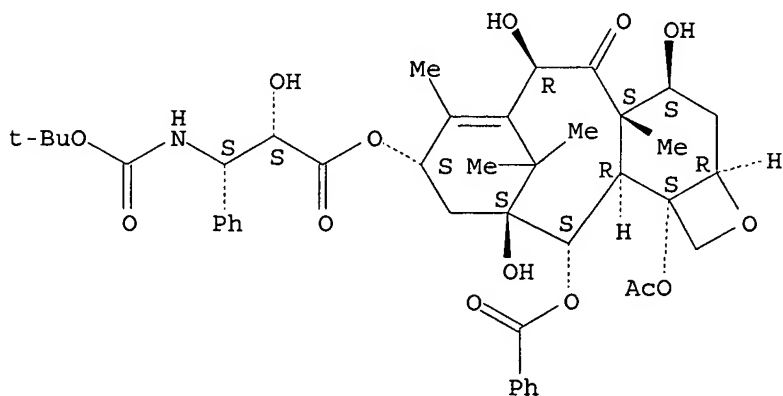
Absolute stereochemistry.



RN 133577-33-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

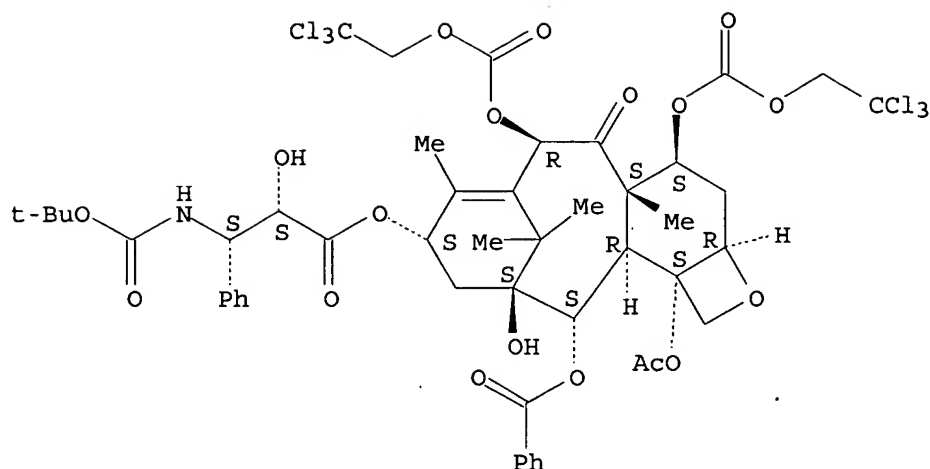
Absolute stereochemistry.



IT 151509-29-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and conformation determined by NMR and mol. modeling)



L51 ANSWER 45 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:8769 CAPLUS

DOCUMENT NUMBER: 120:8769

TITLE: Conformation of Taxotere and analogs determined by NMR spectroscopy and molecular modeling studies

AUTHOR(S): Dubois, Joelle; Guenard, Daniel; Gueritte-Voegelein, Francoise; Guedira, Nourredine; Potier, Pierre; Gillet, Brigitte; Beloeil, Jean Claude

CORPORATE SOURCE: Inst. Chim. Subst. Nat., CNRS, Gif-sur-Yvette, 91198, Fr.

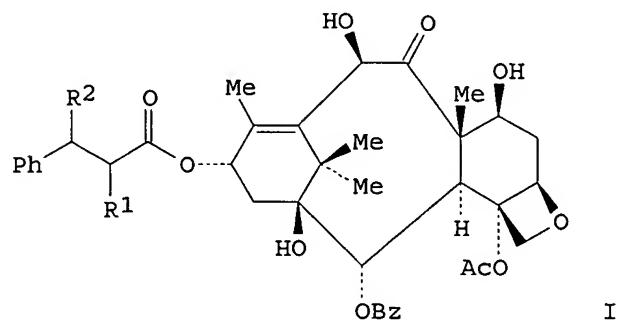
SOURCE: Tetrahedron (1993), 49(30), 6533-44

CODEN: TETRAB; ISSN: 0040-4020

DOCUMENT TYPE: Journal

LANGUAGE: English

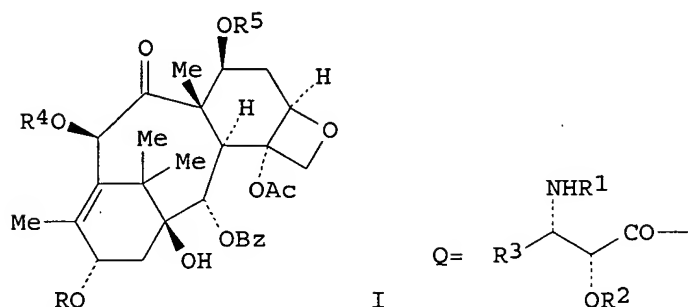
GI



I

AB The conformation of Taxotere (2'R,3'S)-I (R1 = OH, R2 = NHCO2CMe3) and its analogs, (2'R)-I (R1 = OH, R2 = H), (3'R)-I (R1 = H, R2 = NHCO2CMe3), (2'S,3'R)-I (R1 = O2CMe, R2 = NHBz), etc., was determined by NMR spectroscopy and mol. modeling. The most active 2'R,3'S compds. possess a conformation in which the benzoate group at C-2 holds the side chain in a defined position due to hydrophobic interactions between this group and the N-amido or N-carboxyloxy group at C-3'. On the other hand, the 2'S,3'R isomers which display low in vivo biol. activity, such as (2'S,3'R)-I (R1

FI 106959 B1 20010515  
 PRIORITY APPLN. INFO.: FR 1992-1379 A 19920207  
 WO 1993-FR110 A 19930204  
 OTHER SOURCE(S): CASREACT 120:30979; MARPAT 120:30979  
 GI



AB Title compds. (I; R = aminohydroxypropionyl group Q; R1 = Bz, COCMe3; R2 = H; R3 = aryl; R4 = H or Ac; R5 = H) were prepared by condensation of QOH (R2 = hydroxy-protective group) with I (R = H, R4 = Ac or hydroxy-protective group, R5 = hydroxy-protective group). Thus, I (R4 = R5 = CO2CH2CF3) (II; R = H) was stirred 72 h at -10° with (2R,3S)-PhCH(NHCO2CMe3)CH[OCH(OEt)Me]CO2H in PhMe containing DCC and 4-pyrrolidinopyridine to give 97% II [R = COCH(OH)CHPhNCO2CMe3] with 12.7% epimerization at C-2 of the acid moiety.

IT 151636-78-1P

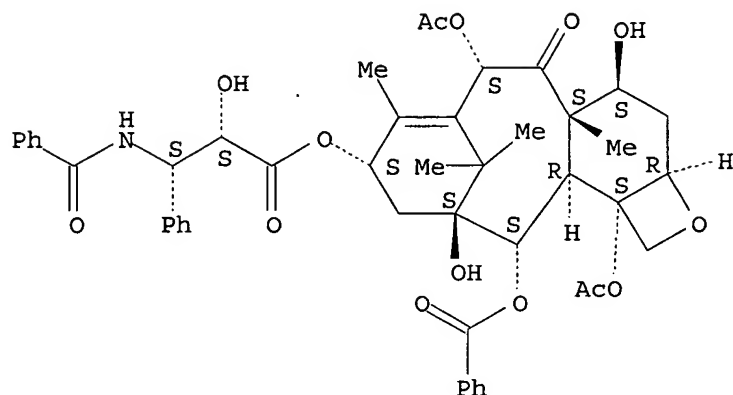
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

RN 151636-78-1 CAPLUS

CN Benzenepropanoic acid, β-[[[(1,1-dimethylethoxy)carbonyl]amino]-α-hydroxy-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4,6-bis[[[(2,2,2-trichloroethoxy)carbonyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4β,4aβ,6β,9α(αS\*,βS\*),11α,12α,12aα,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.



L51 ANSWER 44 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1994:30979 CAPLUS  
 DOCUMENT NUMBER: 120:30979  
 TITLE: Method for preparing taxane derivatives  
 INVENTOR(S): Fouque, Elie; Mas, Jean Manuel  
 PATENT ASSIGNEE(S): Rhone-Poulenc Rorer SA, Fr.  
 SOURCE: PCT Int. Appl., 12 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

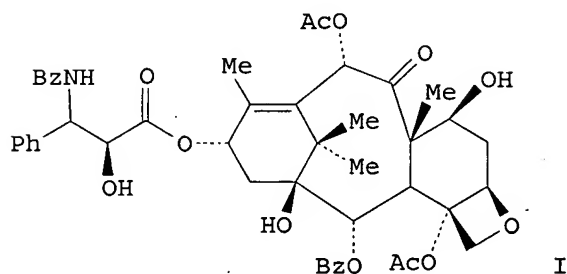
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316059	A1	19930819	WO 1993-FR110	19930204
W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2687150	A1	19930813	FR 1992-1379	19920207
FR 2687150	B1	19950428		
AU 9335048	A1	19930903	AU 1993-35048	19930204
AU 686095	B2	19980205		
EP 625147	A1	19941123	EP 1993-904150	19930204
EP 625147	B1	19960828		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 07503472	T2	19950413	JP 1993-513563	19930204
JP 3295879	B2	20020624		
HU 68773	A2	19950728	HU 1994-2289	19930204
HU 212577	B	19960829		
AT 141920	E	19960915	AT 1993-904150	19930204
ES 2090970	T3	19961016	ES 1993-904150	19930204
RU 2103266	C1	19980127	RU 1994-40356	19930204
CZ 283377	B6	19980415	CZ 1994-1870	19930204
PL 175106	B1	19981130	PL 1993-304721	19930204
SK 280012	B6	19990712	SK 1994-930	19930204
CA 2126462	C	20020709	CA 1993-2126462	19930204
ZA 9300823	A	19930916	ZA 1993-823	19930205
US 6596880	B1	20030722	US 1994-256736	19940802
NO 9402895	A	19940804	NO 1994-2895	19940804
NO 305863	B1	19990809		
FI 9403643	A	19940805	FI 1994-3643	19940805

Correction of: 118:232375

TITLE: Antitumor compound NSC-LSC1 and its manufacture with callus culture of *Taxus brevifolia*  
 INVENTOR(S): Saito, Koji; Ohashi, Hiroaki; Tahara, Makoto; Sakamoto, Tetsuo  
 PATENT ASSIGNEE(S): Nippon Steel Corp., Japan  
 SOURCE: PCT Int. Appl., 1 p.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9302067	A1	19930204	WO 1992-JP917	19920717
W: CA, JP, KR, US				
RW: AT, BE, CH, DE, FR, GB, IT, SE				
CA 2092705	AA	19930118	CA 1992-2092705	19920717
CA 2092705	C	19951107		
EP 555485	A1	19930818	EP 1992-915865	19920717
R: AT, BE, CH, DE, FR, GB, IT, LI, SE				
PRIORITY APPLN. INFO.:			JP 1991-176902	A 19910717
			WO 1992-JP917	W 19920717

GI



AB Low-toxicity, antitumor compound NSC-LSC1 (I), a taxol analog, is manufactured with a callus culture developed from albumens of *Taxus*, especially *Taxus brevifolia*. In vitro antitumor activity of I was shown by its IC<sub>50</sub> of 3.3 and 19 ng/mL against P388 mouse leukemia cells and KB human squamous carcinoma cells, resp.

IT 147557-12-8P

RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)

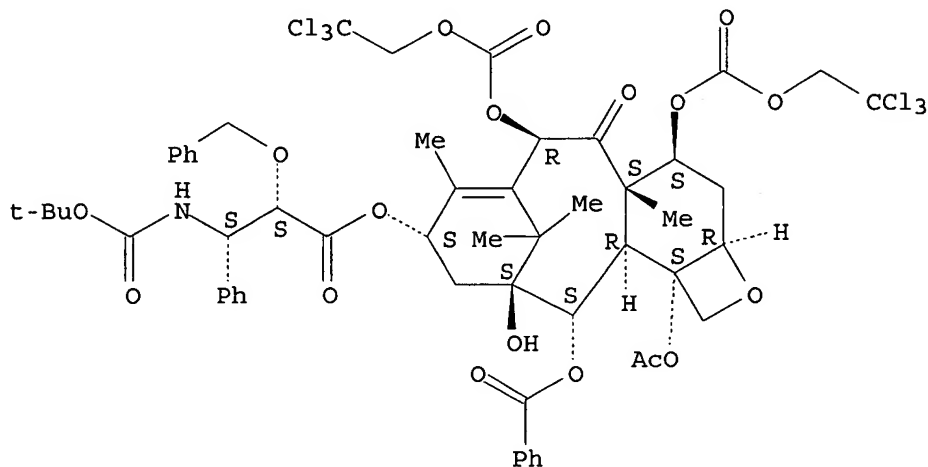
(manufacture of, with callus culture of *Taxus brevifolia*, as antitumor agent)

RN 147557-12-8 CAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2αα,4β,4αβ,6α,9α(αS\*,βS\*),11.alpha.,12α,12αα,12βα]]- (9CI) (CA INDEX NAME)

methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*)],11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 155487-38-0P

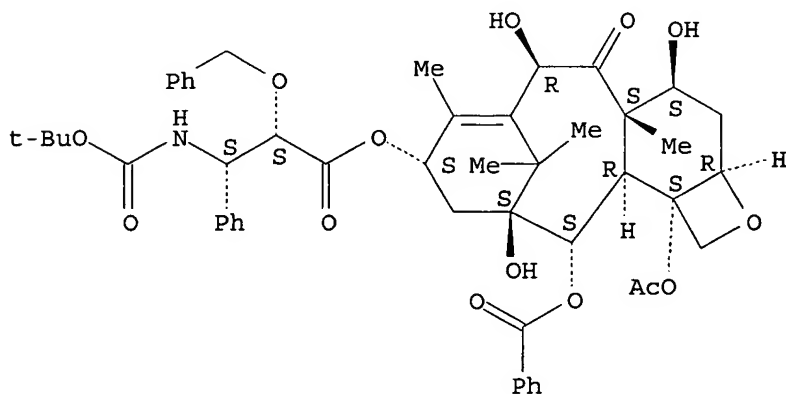
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrogenolysis of, taxotere from)

RN 155487-38-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -(phenylmethoxy)-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

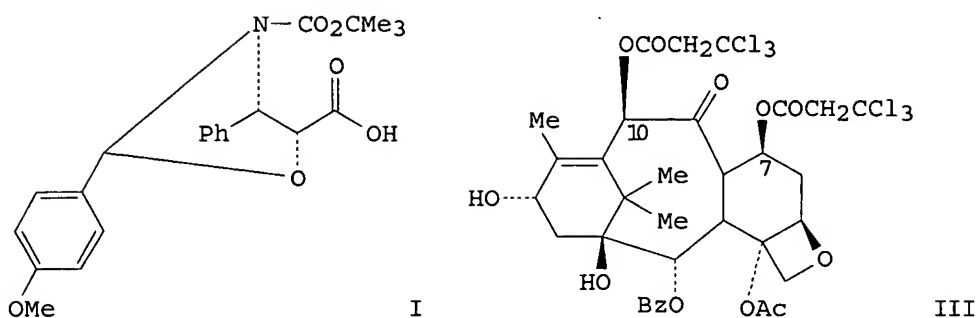


L51 ANSWER 43 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:242670 CAPLUS

Correction of: 1993:232375

DOCUMENT NUMBER: 120:242670



AB A high-yield synthesis of the p-methoxybenzylidene-protected docetaxel (Taxotere) side chain I, a useful derivative for efficient, epimerization-free esterification of the 7,10-bis[(trichloroethoxy)carbonyl] derivative II of 10-desacetylbaccatin III for the preparation of docetaxel, has been effected. The C-4 and C-5 stereocenters of the 1,3-oxazolidine are generated with complete ( $\geq 99\%$ ) stereocontrol whereas that at C-2 is produced with 96% selectivity.

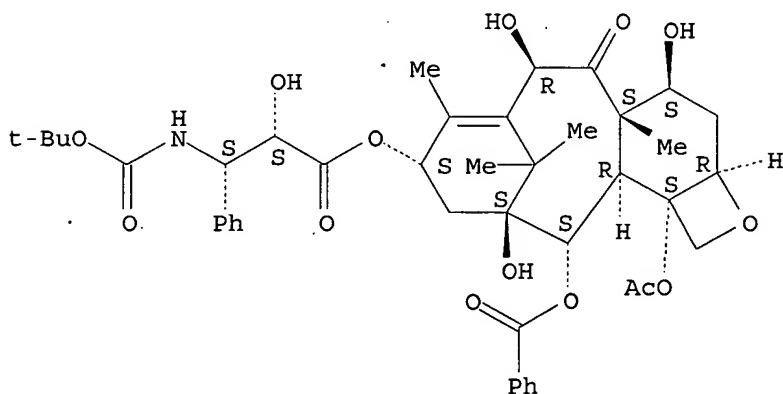
IT 133577-33-0P, 2'-epi-Taxotere

RL: FORM (Formation, nonpreparative); PREP (Preparation)  
(formation of, in synthesis of taxotere)

RN 133577-33-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 155487-37-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and de(trichloroethoxy)carbonylation of, in synthesis of taxotere)

RN 155487-37-9 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -(phenylmethoxy)-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4,6-bis[[(2,2,2-trichloroethoxy)carbonyl]oxy]-7,11-

the same precision as had been possible for taxol, but the conformational possibilities could be significantly limited by the data. Analogs I [(2'R), R = Ac, R1 = H, R2 = NHCO2Bz; (2'R), R = Ac, R1 = Ph, R2 = H; (2'S), R = Ac, R1 = Ph, R2 = H], but not (2'S)-I (R = Ac, R1 = H, R2 = NHCO2Bz), can mimic the dominant conformation of taxol in chloroform, but no logical relationship between biol. activity and aqueous solution conformation could be detected.

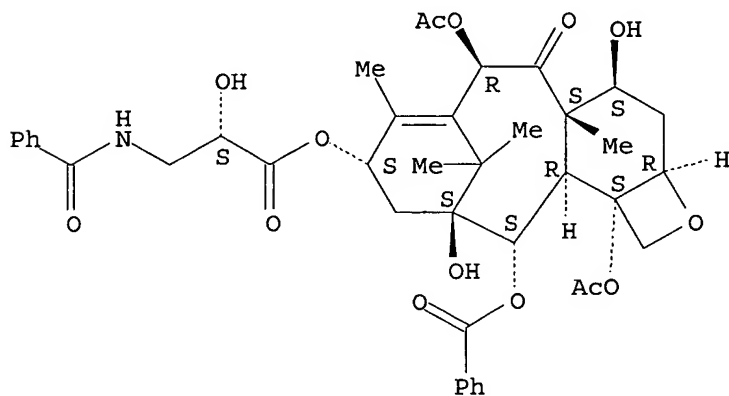
IT 131896-67-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 131896-67-8 CAPLUS

CN Propanoic acid, 3-(benzoylamino)-2-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4β,4aβ,6β,9α(S\*),11.α.,12α,12aα,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 42 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:435897 CAPLUS

DOCUMENT NUMBER: 121:35897

TITLE: Highly Stereocontrolled and Efficient Preparation of the Protected, Esterification-Ready Docetaxel (Taxotere) Side Chain

AUTHOR(S): Kanazawa, Alice M.; Denis, Jean-Noel; Greene, Andrew E.

CORPORATE SOURCE: Universite Joseph Fourier de Grenoble, Grenoble, 38041, Fr.

SOURCE: Journal of Organic Chemistry (1994), 59(6), 1238-40  
CODEN: JOCEAH; ISSN: 0022-3263

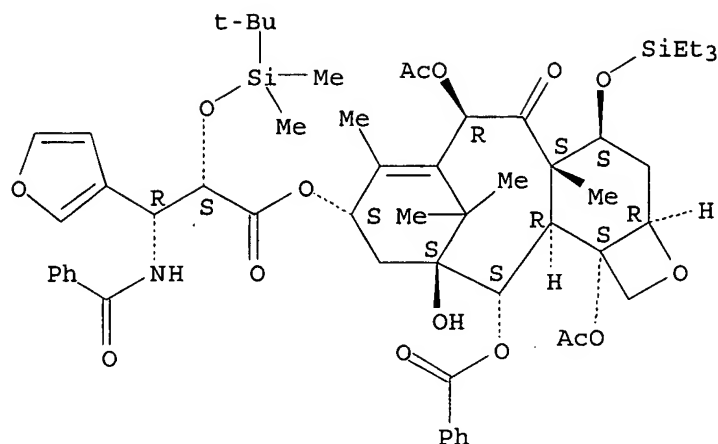
DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 121:35897

GI





L51 ANSWER 41 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:483667 CAPLUS

DOCUMENT NUMBER: 121:83667

TITLE: NMR and molecular modeling study of active and inactive taxol analogs in aqueous and nonaqueous solution

AUTHOR(S): Williams, Howard J.; Scott, A. Ian; Dieden, Reiner A.; Swindell, Charles S.; Chirlian, Lisa E.; Francl, Michelle M.; Heering, Julia M.; Krauss, Nancy E.

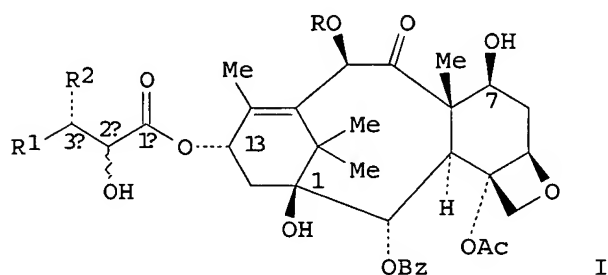
CORPORATE SOURCE: Cent. Biol. NMR, Texas A and M Univ., College Station, TX, 77843-3255, USA

SOURCE: Canadian Journal of Chemistry (1994), 72(1), 252-60  
CODEN: CJCHAG; ISSN: 0008-4042

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB The conformations of the biol. active taxol analogs Taxotere [(2'R)-I; R = H, R1 = Ph, R2 = NHCO2CMe3], (2'R)-I (R = Ac, R1 = H, R2 = NHCO2Bz), (2'R)-I (R = Ac, R1 = Ph, R2 = H), and (2'S)-I (R = Ac, R1 = Ph, R2 = H), and the biol. inactive analog (2'S)-I (R = Ac, R1 = H, R2 = NHCO2Bz) were evaluated in CDCl3 and DMSO-water solution using 1H NMR coupling constant and NOESY data and mol. modeling. The solution structures of Taxotere were very similar to those detected previously for taxol [(2'R)-I; R = Ac, R1 = Ph, R2 = NHCO2Bz]. The A-ring side chain conformations of analogs I (R = Ac, R1 = H, R2 = NHCO2Bz; R = Ac, R1 = Ph, R2 = H) could not be defined with

(R1 = 2-furyl) proved to be more active than the parent, taxol.

IT 158412-29-4P 158412-30-7P

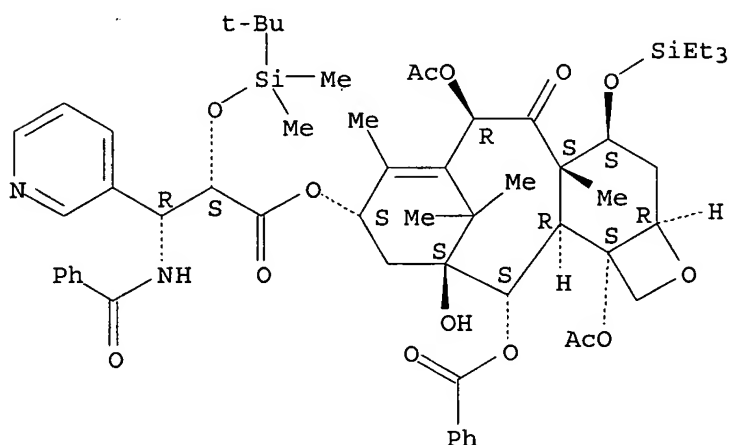
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of taxol analogs)

RN 158412-29-4 CAPLUS

CN 3-Pyridinepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2 $\alpha\alpha$ ,4 $\beta$ ,4 $\alpha\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*)],11 $\alpha$ ,12 $\alpha$ ,12 $\alpha\alpha$ ,12 $\beta\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

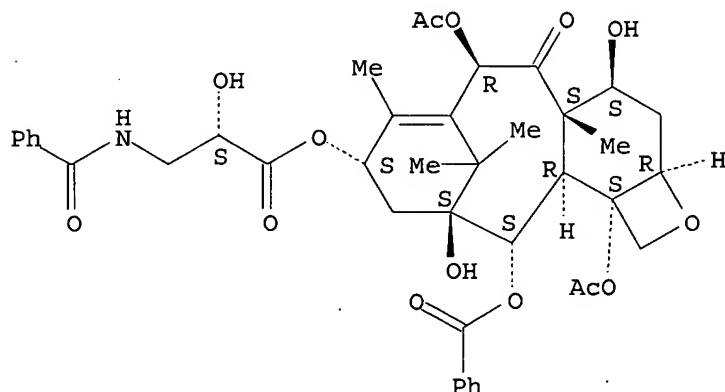


RN 158412-30-7 CAPLUS

CN 3-Furanpropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2 $\alpha\alpha$ ,4 $\beta$ ,4 $\alpha\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*)],11 $\alpha$ ,12 $\alpha$ ,12 $\alpha\alpha$ ,12 $\beta\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.



L51 ANSWER 40 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:656068 CAPLUS

DOCUMENT NUMBER: 121:256068

TITLE: Heteroaromatic taxol analogs: the chemistry and biological activities of 3'-furyl and 3'-pyridyl substituted taxanes

AUTHOR(S): Georg, Gunda I.; Harriman, Geraldine C. B.; Hepperle, Michael; Himes, Richard H.

CORPORATE SOURCE: Dep. Medicinal Chem., Univ. Kansas, Lawrence, KS, 66045, USA

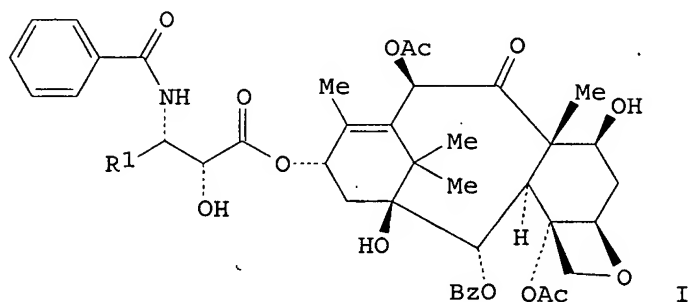
SOURCE: Bioorganic & Medicinal Chemistry Letters (1994), 4(11), 1381-4

CODEN: BMCLE8; ISSN: 0960-894X

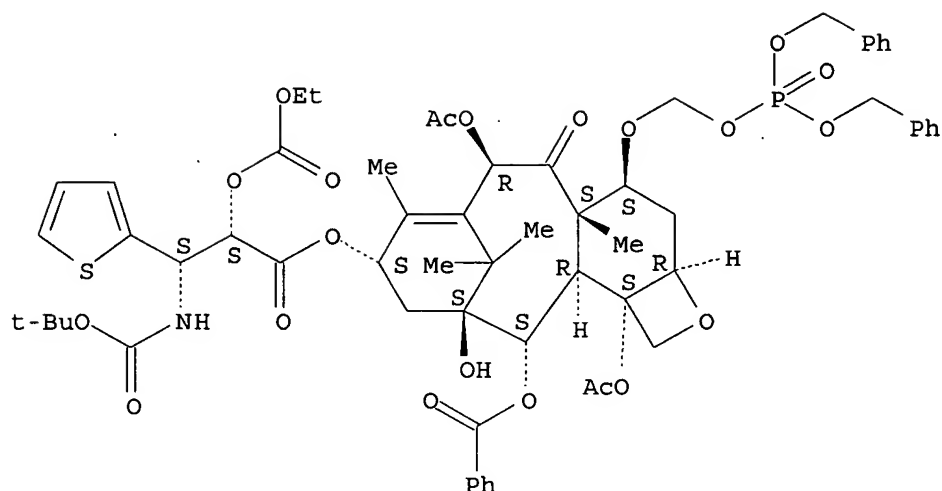
DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB A series of novel heterocyclic taxol analogs I ( $R_1$  = 2-, 3-, 4-pyridyl, 2-, 3-furyl) has been synthesized utilizing 2-azetidinones derived from the ester enolate-imine cyclocondensation. 2-Azetidinones possessing stereochem. complementary to that of taxol's phenylisoserine side chain were synthesized in fair to high enantiomeric purity utilizing the chiral glycolate derived from Oppolzer's chiral auxiliary and the appropriate N-trimethylsilylaldimines. I were evaluated in the microtubule assembly assay as well as tested for cytotoxicity against B16 melanoma cells. I



L51 ANSWER 39 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:209891 CAPLUS

DOCUMENT NUMBER: 122:45673

TITLE: Relationship between the structure of taxol and other taxanes on induction of tumor necrosis factor- $\alpha$  gene expression and cytotoxicity

AUTHOR(S): Burkhardt, Catherine A.; Berman, Joan W.; Swindell, Charles S.; Horwitz, Susan Band

CORPORATE SOURCE: Dep. Mol. Pharmacol., Albert Einstein Coll. Med., Bronx, NY, 10461, USA

SOURCE: Cancer Research (1994), 54(22), 5779-82

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Taxol is an antitumor drug with cytotoxic properties that correlate with its microtubule-stabilizing activities. It has been reported that taxol parallels lipopolysaccharide in its effects on the induction of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) gene expression in macrophages. Structure-activity studies using taxol and related taxanes have been done to determine the relationship between the effects of taxol on TNF- $\alpha$  gene expression and its cytotoxic and microtubule-stabilizing activities. Using Northern blot anal., it was found that changes in the structure of taxol that did not alter cytotoxicity did prevent the induction of TNF- $\alpha$  gene expression. The data presented in this paper demonstrate that the effects of taxol on TNF- $\alpha$  gene expression are distinct from its known cytotoxic properties.

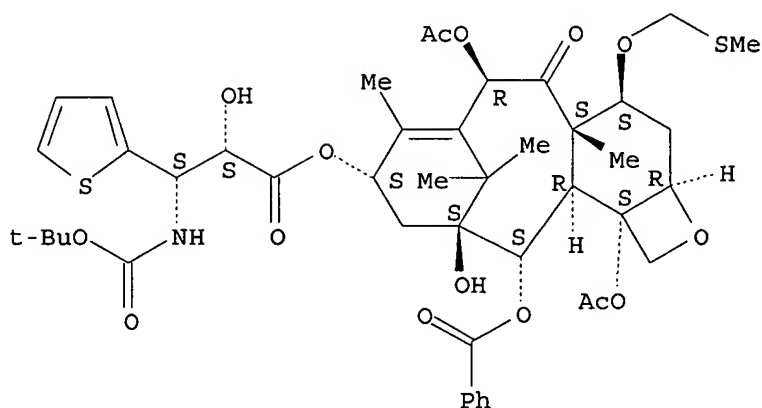
IT 131896-67-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(relationship between structure of taxol and other taxanes on induction of tumor necrosis factor- $\alpha$  gene expression and cytotoxicity)

RN 131896-67-8 CAPLUS

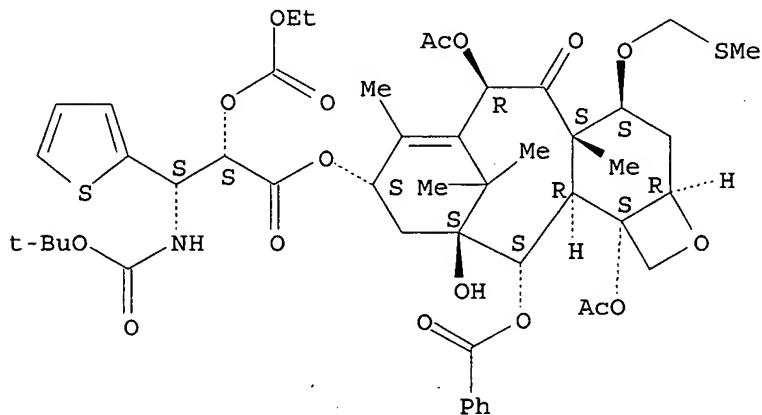
CN Propanoic acid, 3-(benzoylamino)-2-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2 $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ (S\*),11.alpha.,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)



RN 162871-22-9 CAPLUS

CN 2-Thiophenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy) carbonyl] amino] -  
 $\alpha$ -[(ethoxycarbonyl) oxy] -, 6,12b-bis (acetyloxy) -12- (benzoyloxy) -  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-  
 tetramethyl-4- [(methylthio) methoxy] -5-oxo-7,11-methano-1H-  
 cyclodeca [3,4] benz [1,2-b] oxet-9-yl ester, [2aR-  
 [2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*),11 $\alpha$   
 ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 162871-23-0 CAPLUS

CN 2-Thiophenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy) carbonyl] amino] -  
 $\alpha$ -[(ethoxycarbonyl) oxy] -, 6,12b-bis (acetyloxy) -12- (benzoyloxy) -4-  
 [[ [bis (phenylmethoxy) phosphinyl] oxy] methoxy] -2a,3,4,4a,5,6,9,10,11,12,12a,  
 12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-  
 cyclodeca [3,4] benz [1,2-b] oxet-9-yl ester, [2aR-  
 [2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*),11 $\alpha$   
 ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

OTHER SOURCE(S):

MARPAT 122:291219

AB Taxane derivs. T-[OCH<sub>2</sub>(OCH<sub>2</sub>)<sub>m</sub>OP(O)(OH)<sub>2</sub>]<sub>n</sub> [T = taxane substituted at C-13 by 3-amino-2-hydroxypropanoyloxy; m = 0-6; n = 1-3] were prepared from paclitaxel or baccatin III via T'-[OCH<sub>2</sub>(OCH<sub>2</sub>)<sub>m</sub>SMel]<sub>n</sub> [T' = protected T] for use as antitumor agents. Thus, paclitaxel was converted to its 7-O-methylthiomethyl derivative, treated with dibenzyl phosphate, followed by hydrogenolysis to give 7-O-phosphonooxymethylpaclitaxel. This compound had an IC<sub>50</sub> against HCT-116 human carcinoma of 0.0158 μM. Some of the methylthiomethyl derivs. also have antitumor activity.

IT 162871-20-7P 162871-21-8P 162871-22-9P

162871-23-0P

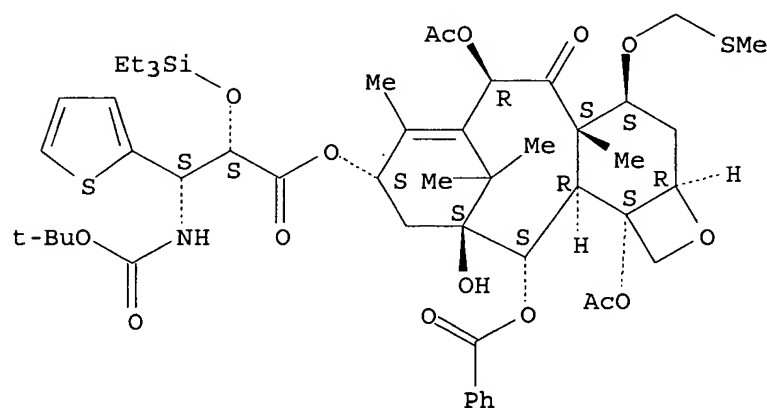
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(phosphonooxymethyl or methylthiomethyl ethers of taxane derivs. as antitumor agents.)

RN 162871-20-7 CAPLUS

CN 2-Thiophenepropanoic acid, β-[[[(1,1-dimethylethoxy)carbonyl]amino]-α-[(triethylsilyl)oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-4-[(methylthio)methoxy]-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4β,4aβ,6β,9α(αS\*,βS\*),11α,12α,12aα,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 162871-21-8 CAPLUS

CN 2-Thiophenepropanoic acid, β-[[[(1,1-dimethylethoxy)carbonyl]amino]-α-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-4-[(methylthio)methoxy]-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4β,4aβ,6β,9α(αS\*,βS\*),11α,12α,12aα,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L51 ANSWER 38 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:526804 CAPLUS

DOCUMENT NUMBER: 122:291219

TITLE: Phosphonooxymethyl or methylthiomethyl ethers of taxane derivatives as antitumor agents.

INVENTOR(S): Golik, Jerzy; Kadow, John F.; Kaplan, Murray A.; Li, Wen-Sen; Perrone, Robert K.; Thottathil, John K.; Vyas, Dolatrai; Wittman, Mark D.; Wong, Henry; Wright, John J.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA

SOURCE: Eur. Pat. Appl., 124 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 639577	A1	19950222	EP 1994-112803	19940816
EP 639577	B1	20020515		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
IL 122990	A1	20020523	IL 1993-122990	19931223
IL 148029	A1	20050517	IL 1993-148029	19931223
CA 2129288	AA	19950218	CA 1994-2129288	19940802
CA 2129288	C	20000516		
HU 67742	A2	19950428	HU 1994-2342	19940812
JP 07149779	A2	19950613	JP 1994-250219	19940812
JP 3062986	B2	20000712		
FI 9403749	A	19950218	FI 1994-3749	19940815
FI 113271	B1	20040331		
NO 9403002	A	19950220	NO 1994-3002	19940815
NO 309093	B1	20001211		
AU 9470267	A1	19950302	AU 1994-70267	19940815
AU 694941	B2	19980806		
CN 1111637	A	19951115	CN 1994-109468	19940815
CN 1051315	B	20000412		
RU 2128661	C1	19990410	RU 1994-29662	19940815
ZA 9406180	A	19950216	ZA 1994-6180	19940816
PL 179636	B1	20001031	PL 1994-304649	19940816
AT 217629	E	20020615	AT 1994-112803	19940816
PT 639577	T	20021031	PT 1994-112803	19940816
ES 2176212	T3	20021201	ES 1994-112803	19940816
US 5646176	A	19970708	US 1995-445360	19950519
US 2001023255	A1	20010920	US 1997-870794	19970606
US 6455575	B2	20020924		
AU 9891356	A1	19990114	AU 1998-91356	19981106
AU 706511	B2	19990617		
CN 1237580	A	19991208	CN 1999-105343	19990429
CN 1100771	B	20030205		
PRIORITY APPLN. INFO.:			US 1993-108015	A 19930817
			US 1993-154840	A 19931124
			US 1994-245119	A 19940517
			US 1992-996455	B2 19921224
			IL 1993-108161	A3 19931223
			IL 1993-122990	A3 19931223
			AU 1994-70267	A3 19940815
			US 1995-427502	B1 19950424

RN 168416-36-2 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[1,1-dimethylethoxy)carbonyl]amino]-  
 $\alpha$ -hydroxy- $\alpha$ -methyl-, 12b-(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-4,6-bis[[[2,2,2-trichloroethoxy)carbonyl]oxy]-7,11-  
 methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-  
 [2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9a( $\alpha$ S\*, $\beta$ R\*)],11 $\alpha$   
 ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

The chemical structure is a complex polycyclic molecule, likely a steroid or a similar terpenoid derivative. It features a central polycyclic core with several stereocenters indicated by wedges and dashes. The structure includes various functional groups and substituents:

- Left side:** A *t*-BuO-C(=O)-NH- group is attached to a chiral center (R). This center is also bonded to a phenyl group (Ph) and a methyl group (Me). The methyl group is further bonded to a chiral center (S) which has a hydroxyl group (OH) and a carboxylate group (-C(=O)O-).
- Top:** A carboxylate group (-C(=O)O-) is attached to a chiral center (R). This center is also bonded to a methyl group (Me) and a carboxylate group (-C(=O)O-). The carboxylate group is further bonded to a chiral center (S) which has a hydroxyl group (OH) and a carboxylate group (-C(=O)O-).
- Right side:** A carboxylate group (-C(=O)O-) is attached to a chiral center (R). This center is also bonded to a methyl group (Me) and a carboxylate group (-C(=O)O-). The carboxylate group is further bonded to a chiral center (S) which has a hydroxyl group (OH) and a carboxylate group (-C(=O)O-).
- Bottom:** A carboxylate group (-C(=O)O-) is attached to a chiral center (R). This center is also bonded to a methyl group (Me) and a carboxylate group (-C(=O)O-). The carboxylate group is further bonded to a chiral center (S) which has a hydroxyl group (OH) and a carboxylate group (-C(=O)O-).

The structure is highly complex and contains many stereocenters, making it difficult to represent accurately with a single chemical formula. The labels R and S indicate the stereochemistry at various chiral centers.

IT 168416-30-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(novel niobium chloride-based stereoselective approach to  
methyldocetaxel)

RN 168416-30-6 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-  
 $\alpha$ -hydroxy- $\alpha$ -methyl-, 12b-(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
 ester, [2aR, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R  
 \*) ,11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]]- (9CI) (CA INDEX NAME)

The chemical structure shows a complex molecule with a linker group on the left and a complex polycyclic system on the right. The linker group consists of a tert-butoxy carbonyl group (t-BuO-C(=O)-) connected to an amide group (-NH-), which is further connected to a chiral center (CH) bearing a phenyl group (Ph) and a methyl group (Me). This chiral center is connected to another chiral center (CH) bearing a hydroxyl group (OH) and a methyl group (Me). This second chiral center is connected to an ester group (-C(=O)-O-), which is linked to the polycyclic system. The polycyclic system is a complex of fused rings, including a cyclohexene ring and a bicyclic system. It features several substituents: a methyl group (Me) on the cyclohexene ring, a hydroxyl group (OH) on a ring, a phenyl ester group (Ph-C(=O)-O-) on a ring, and an acetoxy group (AcO) on a ring. The structure also includes several stereocenters marked with 'R' and 'S' and various other functional groups like carbonyls and hydroxyls.



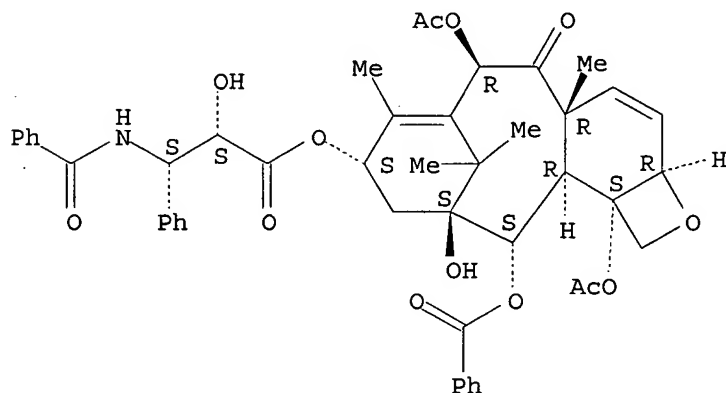
AB Taxane derivs. I (R1 = OR or R; R = C1-C6 alkyl, C2-C5 alkenyl; R2 = H or Ac), modified in the 6-7 positions, are antitumor agents. A procedure for the preparation of I and their 2'-epimers is also claimed.

IT 172586-63-9P, 7-Deoxy-2'-epi-taxol-6-ene  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of unsatd. taxane derivs. as antitumor agents)

RN 172586-63-9 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,4a,5,6,9,10,11,12,12a,12b-decahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2 $\alpha$ a,4 $\alpha$  $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*),11 $\alpha$ ,12. $\alpha$ ph a.,12 $\alpha$ a,12 $\beta$ a]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51. ANSWER 37 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:722745 CAPLUS

DOCUMENT NUMBER: 123:228561

TITLE: Docetaxel (taxotere) derivatives: novel NbCl<sub>3</sub>-based stereoselective approach to 2'-methyl docetaxel

AUTHOR(S): Denis, Jean-Noel; Fkyerat, Abdellatif; Gimbert, Yves; Coutterez, Claire; Mantellier, Pierre; Jost, Sylvie; Greene, Andrew E.

CORPORATE SOURCE: LEDSS, Univ. J. Fourier, Grenoble, 38041, Fr.

SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1995), (14), 1811-15  
 CODEN: JCPRB4; ISSN: 0300-922X

PUBLISHER: Royal Society of Chemistry

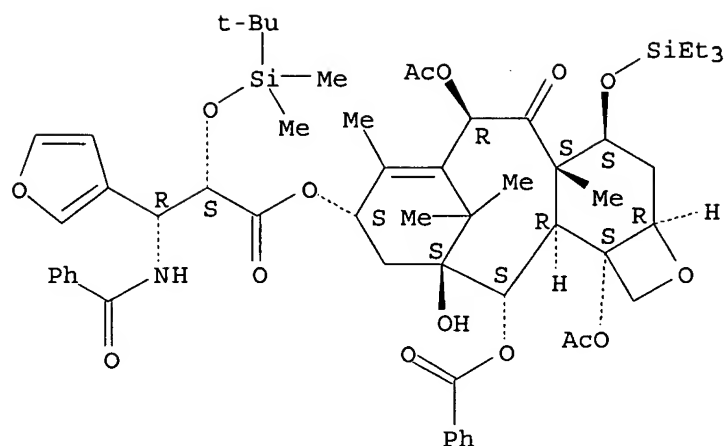
DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 123:228561

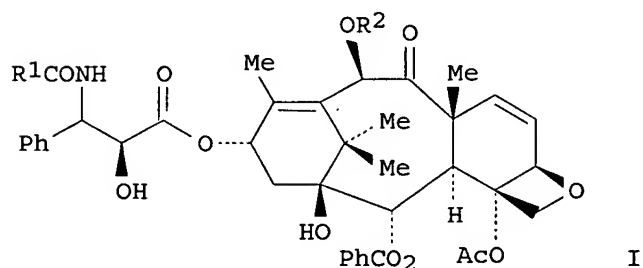
AB The C-2 methylated 2S,3R and 2R,3S side chains of docetaxel have been enantioselectively prepared and esterified with protected 10-deacetylbaccatin III to provide novel analogs of docetaxel.

IT 168416-36-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (novel niobium chloride-based stereoselective approach to



L51 ANSWER 36 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1995:998252 CAPLUS  
 DOCUMENT NUMBER: 124:87428  
 TITLE: Unsaturated taxane derivatives.  
 INVENTOR(S): Mongelli, Nicola; Menichincheri, Maria; Fusar Bassini, Domenico; Ciomei, Marina  
 PATENT ASSIGNEE(S): Pharmacia S.p.A., Italy  
 SOURCE: Ger. Offen., 8 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19516631	A1	19951116	DE 1995-19516631	19950505
GB 2289277	A1	19951115	GB 1995-9353	19950509
GB 2289277	B2	19980819		
JP 07304761	A2	19951121	JP 1995-110678	19950509
PRIORITY APPLN. INFO.:			GB 1994-9131	A 19940509
OTHER SOURCE(S):	CASREACT 124:87428; MARPAT 124:87428			
GI				



pentyl), and N-debenzoyl-N-(3-furoyl)paclitaxel (IV; R2 = 3-furyl) were found to be more cytotoxic than paclitaxel against this cell line.

3'-Dephenyl-3'-(4-pyridyl)paclitaxel (II; R = 4-pyridyl) and N-debenzoyl-N-(2-furoyl)paclitaxel (IV; R2 = 2-furyl) displayed cytotoxicity against B16 melanoma cells similar to paclitaxel.

IT 158412-29-4P 158412-30-7P

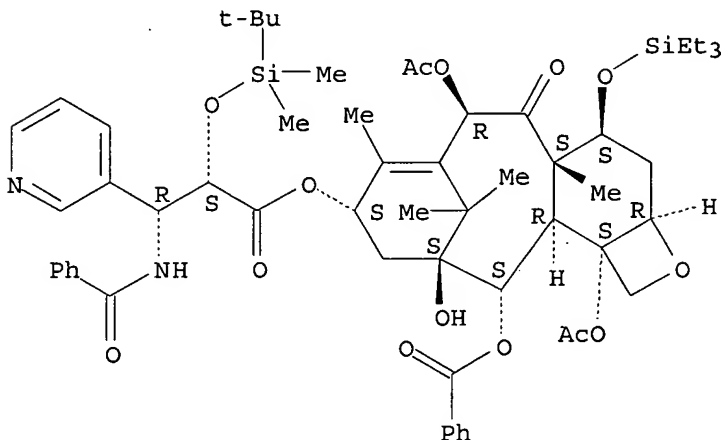
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(asym. synthesis, conformational anal., and biol. evaluation of heteroarom. taxanes)

RN 158412-29-4 CAPLUS

CN 3-Pyridinepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

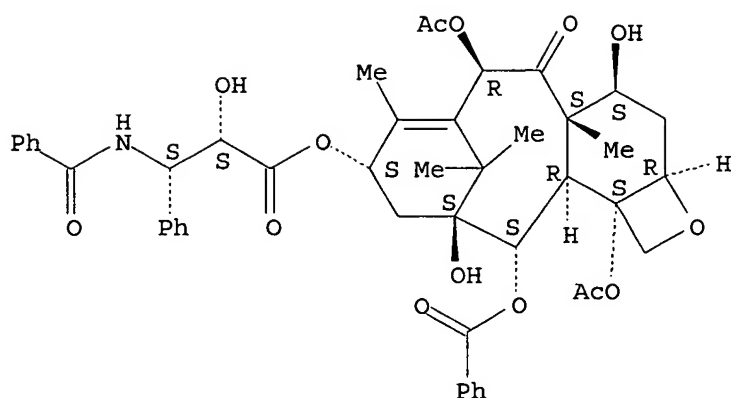
Absolute stereochemistry.



RN 158412-30-7 CAPLUS

CN 3-Furanpropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



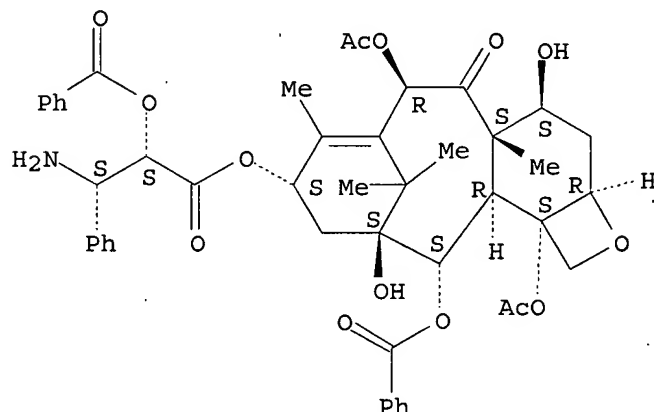
L51 ANSWER 35 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:191997 CAPLUS  
 DOCUMENT NUMBER: 124:317514  
 TITLE: Synthesis, Conformational Analysis, and Biological Evaluation of Heteroaromatic Taxanes  
 AUTHOR(S): Georg, Gunda I.; Harriman, Geraldine C. B.; Hepperle, Michael; Clowers, Jamie S.; Vander Velde, David G.; Himes, Richard H.  
 CORPORATE SOURCE: Department of Medicinal Chemistry, University of Kansas, Lawrence, KS, 66045, USA  
 SOURCE: Journal of Organic Chemistry (1996), 61(8), 2664-76  
 CODEN: JOCEAH; ISSN: 0022-3263  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 124:317514  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The asym. syntheses of heteroarom. 3-[(tert-butyldimethylsilyl)oxy]-2-azetidinones I (R = 2-, 3-, 4-pyridyl, 2-, 3-furyl) via chiral ester enolate-imine cyclocondensation chemical are described. The azetidinones contain heteroarom. moieties which, in certain cases, contribute to a decrease in enantioselectivity due to possible alternate coordinations in the transition states. The (3R,4S)-3-[(tert-butyldimethylsilyl)oxy]-4-heteroaryl-2-azetidinones I were subsequently converted to the heteroarom. taxanes II and III (R1 = OCMe3, pentyl, nonyl). Conformational analyses of the 3'-(2-pyridyl) analog II (R = 2-pyridyl) and 3'-(2-furyl) analog III (R1 = OCMe3) indicate they have solution conformational preferences virtually identical to paclitaxel and docetaxel. Heteroarom. N-acyl paclitaxel analogs IV (R2 = 2-, 3-, 4-pyridyl, 2-, 3-furyl) were prepared from N-debenzoylpaclitaxel via Schotten-Baumann acylation. The majority of the 14 analogs displayed good to excellent activity in a microtubule assembly assay in comparison to paclitaxel. The analogs were also tested for cytotoxicity against B16 melanoma cells. 3'-Dephenyl-3'-(2-pyridyl)paclitaxel (II; R = 2-pyridyl), 3'-dephenyl-3'-(2-furyl)paclitaxel (II; R = 2-furyl), N-BOC-3'-dephenyl-3'-(2-furyl)paclitaxel (III; R = OCMe3), 3'-dephenyl-3'-(2-furyl)-N-(hexanoyl)paclitaxel (III; R1 =

AUTHOR(S): Cabri, Walter  
 CORPORATE SOURCE: Chemical Res. & Development, Bristol-Myers Squibb, Sermoneta, 04010, Italy  
 SOURCE: Tetrahedron Letters (1996), 37(27), 4785-4786  
 CODEN: TELEAY; ISSN: 0040-4039  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 125:143070  
 AB A new 2-step synthesis of 2'-epi-Taxol starting from natural Taxol is described. The approach is centered on the formation of oxazoline on the side chain with concomitant inversion of C-2' followed by acid hydrolysis.  
 IT 179551-57-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (high yield semisynthetic approach to 2'-epi-taxol)  
 RN 179551-57-6 CAPLUS  
 CN Benzenepropanoic acid,  $\beta$ -amino- $\alpha$ -(benzoyloxy)-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, hydrochloride, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



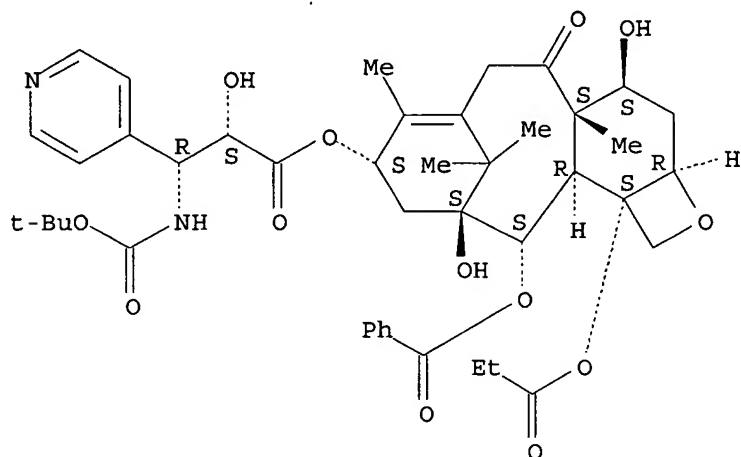
● HCl

IT 179798-21-1P, 2'-epi-Taxol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (high yield semisynthetic approach to 2'-epi-taxol)  
 RN 179798-21-1 CAPLUS  
 CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-12b-(1-oxopropoxy)-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*)],11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

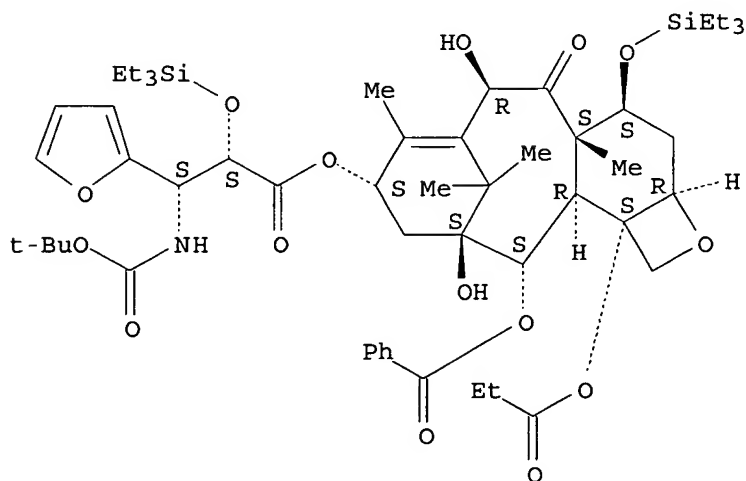
Absolute stereochemistry.



RN 184760-09-6 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -[(triethylsilyl)oxy]-, 12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-6,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-12b-(1-oxopropoxy)-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*)],11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 34 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

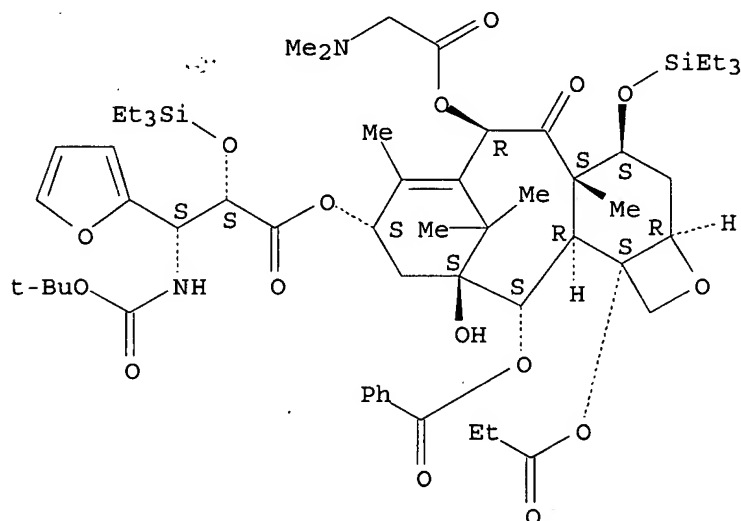
ACCESSION NUMBER: 1996:427283 CAPLUS

DOCUMENT NUMBER: 125:143070

TITLE: A high yield semisynthetic approach to 2'-epi-Taxol

(benzoyloxy)-9-[(2S,3S)-3-[[[(1,1-dimethylethoxy) carbonyl] amino]-3-(2-furanyl)-1-oxo-2-[(triethylsilyl)oxy]propoxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-12b-(1-oxopropoxy)-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-6-yl ester (9CI) (CA INDEX NAME)

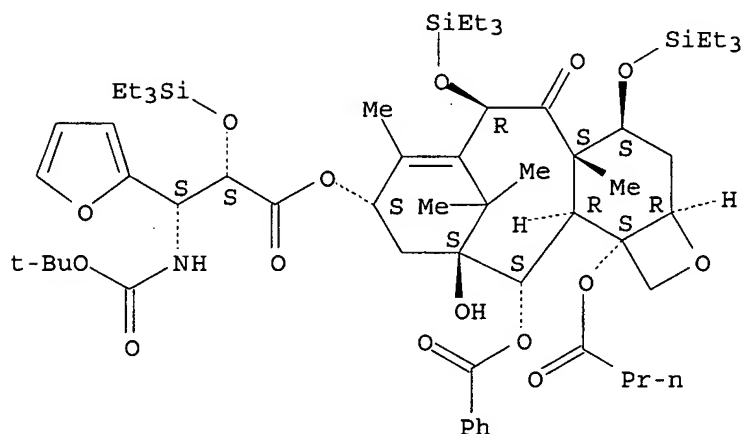
Absolute stereochemistry.



RN 184760-07-4 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy) carbonyl] amino]- $\alpha$ -[(triethylsilyl)oxy]-, 12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-12b-(1-oxobutoxy)-4,6-bis[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

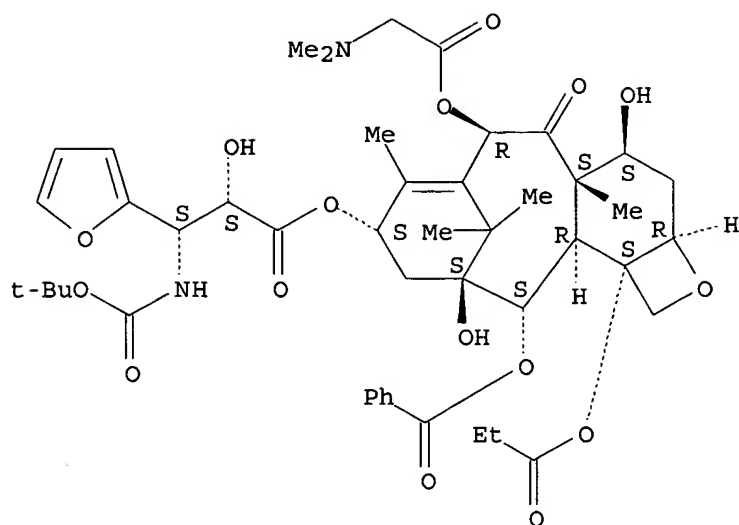


RN 184760-08-5 CAPLUS

CN 4-Pyridinepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy) carbonyl] amino]- $\alpha$ -hydroxy-, 12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-

NAME)

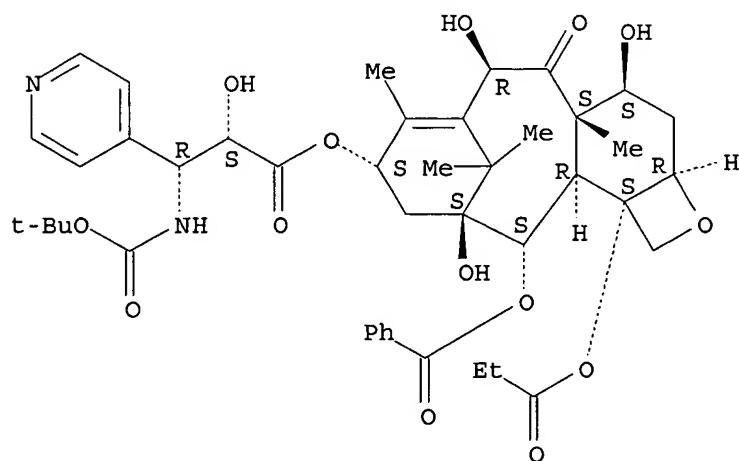
Absolute stereochemistry.



RN 184864-49-1 CAPLUS

CN 4-Pyridinepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, 12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-12b-(1-oxopropoxy)-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*)],11.a lpha.,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 184760-06-3P 184760-07-4P 184760-08-5P

184760-09-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of baccatin III derivs. as antitumors)

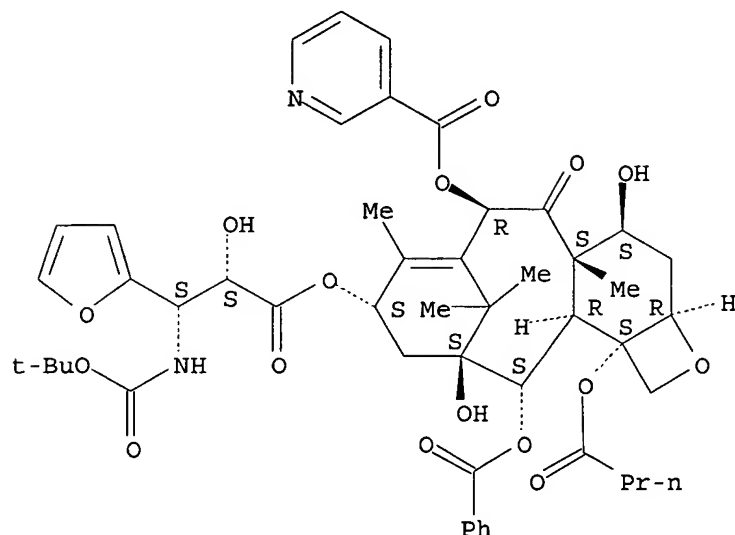
RN 184760-06-3 CAPLUS

CN Glycine, N,N-dimethyl-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12-



b]oxet-6-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ (2S\*,3S\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

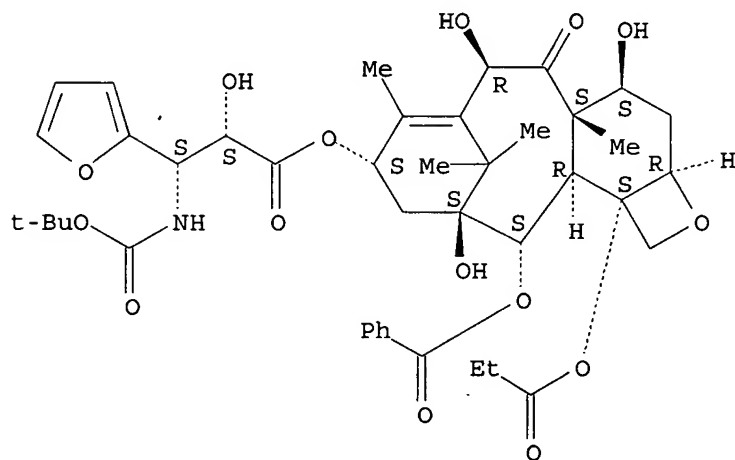
Absolute stereochemistry.



RN 184760-03-0 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, 12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-12b-(1-oxopropoxy)-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*),11.α1pha.,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 184760-04-1 CAPLUS

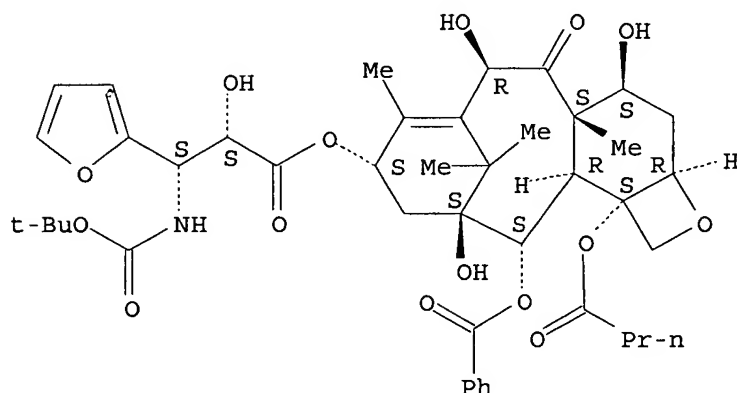
CN Glycine, N,N-dimethyl-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12-(benzoyloxy)-9-[[[(1,1-dimethylethoxy)carbonyl]amino]-3-(2-furanyl)-2-hydroxy-oxopropoxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-12b-(1-oxopropoxy)-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-6-yl ester (9CI) (CA INDEX NAME)

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of baccatin III derivs. as antitumors)

RN 184759-99-7 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-  
 $\alpha$ -hydroxy-, 12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-  
dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-12b-(1-  
oxobutoxy)-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,  
[2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*)],11.a  
lpha.,12 $\alpha$ ,12a,12b $\alpha$ ]]-(9CI) (CA INDEX NAME)

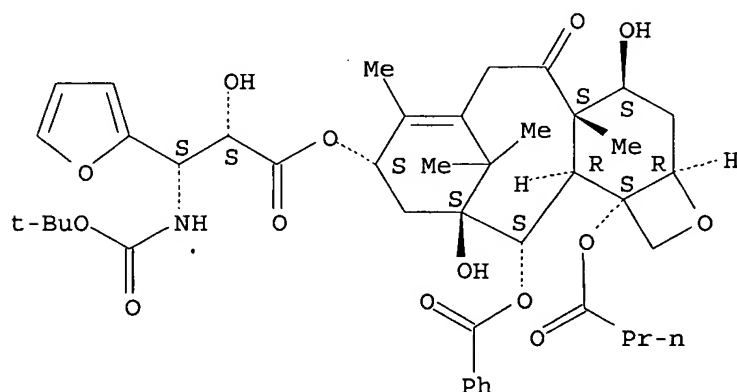
Absolute stereochemistry.



RN 184760-01-8 CAPLUS

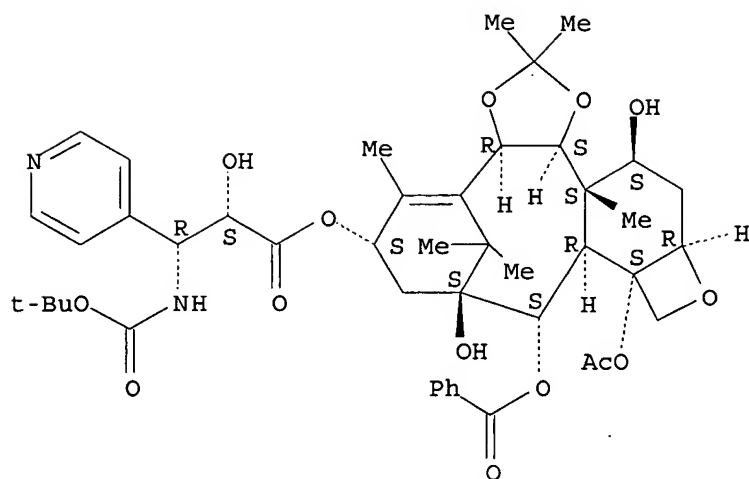
CN 2-Furanpropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-  
 $\alpha$ -hydroxy-, 12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-  
dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-12b-(1-oxobutoxy)-  
7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester,  
[2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*)],11 $\alpha$ ,12  
 $\alpha$ ,12a,12b $\alpha$ ]]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 184760-02-9 CAPLUS

CN 3-Pyridinecarboxylic acid, 12-(benzoyloxy)-9-[3-[[[(1,1-  
dimethylethoxy)carbonyl]amino]-3-(2-furanyl)-2-hydroxy-1-oxopropoxy]-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-12b-(1-oxobutoxy)-7,11-methano-1H-cyclodeca[3,4]benz[1,2-



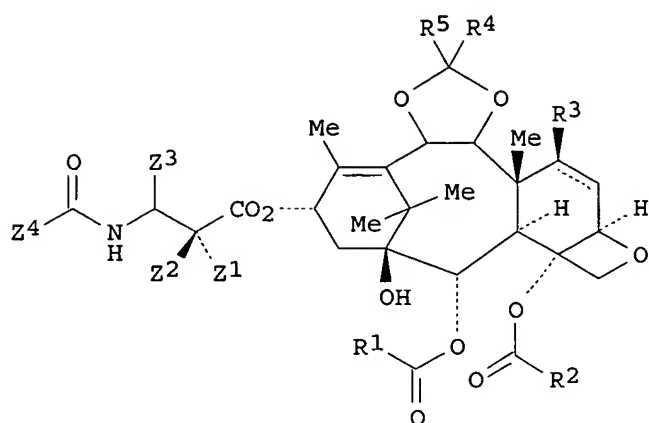
L51 ANSWER 33 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1997:20747 CAPLUS  
 DOCUMENT NUMBER: 126:60178  
 TITLE: Preparation of baccatin III derivatives as antitumors  
 INVENTOR(S): Terasawa, Hirofumi; Soga, Tsunehiko; Uoto, Koichi  
 PATENT ASSIGNEE(S): Daiichi Seiyaku Co, Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 57 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08253465	A2	19961001	JP 1995-58508	19950317
PRIORITY APPLN. INFO.:			JP 1995-58508	19950317
OTHER SOURCE(S):			MARPAT 126:60178	
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. [I; R1 = (un)substituted alkyl, etc.; R2 = H, (un)substituted alkyl, etc.; R3 = H, OH, -CO-R9, etc.; R9 = alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, etc.; R4 = H, OH, halo, alkyl; R5 = H, halo, alkyl; R6 = alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, etc.; R7 = alkyl, aryl, alkoxy; R8 = H, OH] and their pharmaceutically acceptable salts, useful as antitumors, are prepared. Thus, II was prepared in 5 steps from 10-deacetyl-7,10-bis-O-(triethylsilyl)baccatin III via oxidation, alkylation with MeI, reduction, reaction with (2S,3S)-N-(tert-butoxycarbonyl)-N,O-isopropylidene-3-phenylisoserine, and desilylation. In an in vitro study, II had a GI50 0.260 ng/mL against mouse leukemia cells P388.

IT 184759-99-7P 184760-01-8P 184760-02-9P  
 184760-03-0P 184760-04-1P 184864-49-1P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological



I

AB The title compds. [I; R1 = (un)substituted phenyl; R2 = alkyl, alkenyl, alkynyl, cycloalkyl or alkoxy; R3 = H, OH, halo, alkoxy, -CO-R31, etc.; R31 = alkylamino, alkenyl, alkynyl, cycloalkyl, aryl or a heterocycle; R4, R5 = H, alkyl, alkenyl, alkynyl, aryl, heterocyclyl; Z1 = H, OH, halo, alkyl; Z2 = H, OH, halo or alkyl; Z3 = alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, etc.; Z4 = alkyl, aryl, alkoxy, etc.] and their pharmaceutically acceptable salts, useful as antitumors, are prepared. Thus, 10-deacetylbaecatin III was converted into 9 $\beta$ ,13-O-[(2R,3R)-3-(tert-butoxycarbonylamino)-3-(2-furyl)-2-hydroxypropionyl]-10-deacetyl-9-deacetyl-9-dihydro-9,10-O-isopropylidenebaecatin III via the intermediates 9 $\beta$ -10-deacetyl-9-dihydrobaecatin III, 9 $\beta$ -10-deacetyl-9-dihydro-9,10-O-isopropylidenebaecatin III, and 9 $\beta$ -13-O-[(2R,3R)-3-(tert-butoxycarbonylamino)-3-(2-furyl)-2-(triisopropylsilyloxy)propionyl]-10-deacetyl-9-dihydro-9,10-O-isopropylidenebaecatin III. In an in vitro study, I [R1 = Ph, R2 = Pr, R3 =  $\beta$ -OH, R4 = morpholinomethyl, Z1 = OH, Z2 = H, Z3 = 2-furyl, Z4 = tert-butoxy] (also prepared) had an IC<sub>50</sub> of 4.36 ng/mL against mouse leukemia cells P388.

IT 184759-16-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of baecatin III derivs. as antitumors)

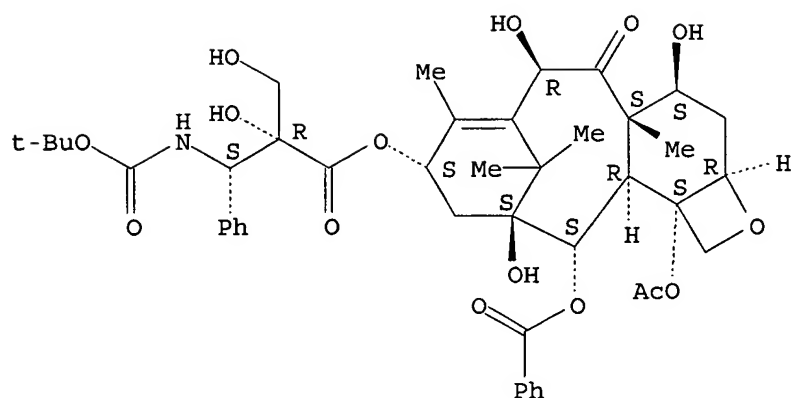
RN 184759-16-8 CAPLUS

CN 4-Pyridinepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, 2a-(acetyloxy)-3-(benzoyloxy)-  
2a,2b,3,4,5,6,8a,11a,11b,12,13,13a-dodecahydro-4,12-dihydroxy-  
7,10,10,11b,14,14-hexamethyl-4,8-methano-2H-oxeto[3'',2':3',4']benzo[1',2':3,4]cyclodeca[1,2-d][1,3]dioxol-6-yl ester, [2aS-[2a $\alpha$ ,2b $\alpha$ ,3 $\alpha$ ,4 $\alpha$ ,6 $\alpha$ ( $\alpha$ R\*, $\beta$ S\*)],8a.alp ha.,11a $\alpha$ ,11b $\beta$ ,12 $\beta$ ,13a $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 173 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633998	A1	19961031	WO 1996-JP1145	19960425
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IS, JP, KG, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AZ, BY, KZ, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2219675	AA	19961031	CA 1996-2219675	19960425
AU 9655145	A1	19961118	AU 1996-55145	19960425
AU 704198	B2	19990415		
EP 826688	A1	19980304	EP 1996-912252	19960425
EP 826688	B1	20010905		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, EE, SI, LT, LV, FI				
CN 1188477	A	19980722	CN 1996-194915	19960425
CN 1094940	B	20021127		
BR 9608040	A	19990112	BR 1996-8040	19960425
AT 205213	E	20010915	AT 1996-912252	19960425
ES 2164241	T3	20020216	ES 1996-912252	19960425
PT 826688	T	20020228	PT 1996-912252	19960425
TW 480262	B	20020321	TW 1996-85104983	19960425
JP 09012578	A2	19970114	JP 1996-106615	19960426
JP 3746563	B2	20060215		
NO 9704912	A	19971229	NO 1997-4912	19971024
NO 321942	B1	20060724		
US 6075140	A	20000613	US 1998-945276	19980205
HK 1008529	A1	20020328	HK 1998-109471	19980728
US 6211363	B1	20010403	US 2000-513852	20000225
US 2001041796	A1	20011115	US 2001-759378	20010116
US 6545151	B2	20030408		
US 2003162971	A1	20030828	US 2002-126653	20020422
US 6646123	B2	20031111		
PRIORITY APPLN. INFO.:			JP 1995-106295	A 19950428
			WO 1996-JP1145	W 19960425
			US 1998-945276	A1 19980205
			US 2000-513852	A1 20000225
			US 2001-759378	A3 20010116
OTHER SOURCE(S):			MARPAT 126:60179	
GI				



IT 186371-29-9P

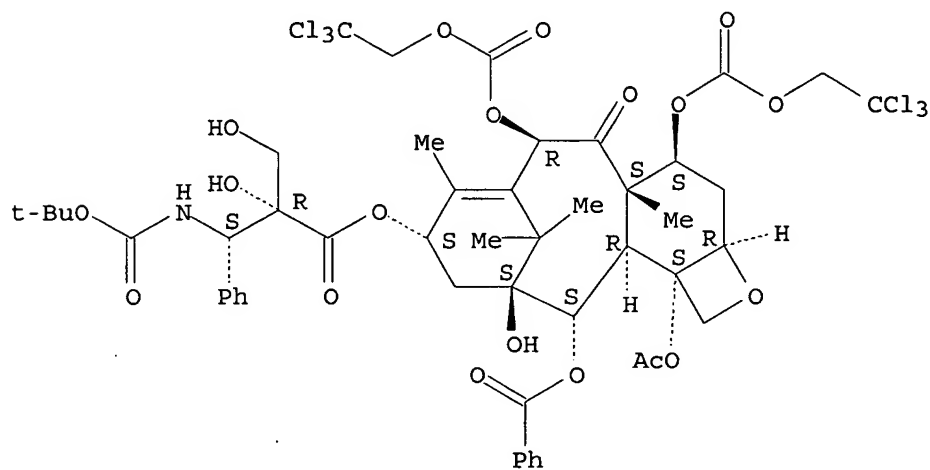
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(asym. Baylis-Hillman-like reaction to prepare  $\alpha$ -aminoalkylacrylic acid derivs. in synthesis of docetaxel hydroxymethyl analogs)

RN 186371-29-9 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy- $\alpha$ -(hydroxymethyl)-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4,6-bis[[[(2,2,2-trichloroethoxy)carbonyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ R\*, $\beta$ S\*)],11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT:

17

THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 32 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

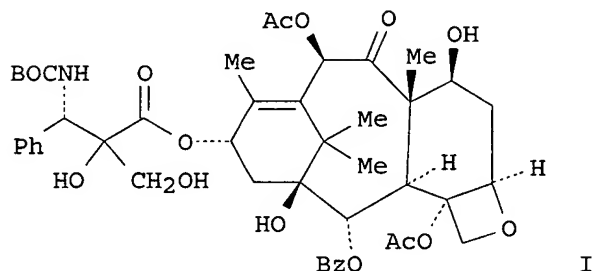
ACCESSION NUMBER: 1997:33889 CAPLUS

DOCUMENT NUMBER: 126:60179

TITLE: Preparation of baccatin III derivatives as antitumors

INVENTOR(S): Terasawa, Hirofumi; Soga, Tsunehiko; Ishiyama, Takashi

ACCESSION NUMBER: 1997:56511 CAPLUS  
 DOCUMENT NUMBER: 126:131656  
 TITLE: Effective enantioselective approach to  
 $\alpha$ -aminoalkylacrylic acid derivatives via a  
 synthetic equivalent of an asymmetric Baylis-Hillman  
 reaction: application to the synthesis of two C-2  
 hydroxymethyl analogs of docetaxel  
 AUTHOR(S): Genisson, Yves; Massardier, Christine; Gautier-Luneau,  
 Isabelle; Greene, Andrew E.  
 CORPORATE SOURCE: LEDSS, Univ. Joseph Fourier, Grenoble, 38041, Fr.  
 SOURCE: Journal of the Chemical Society, Perkin Transactions  
 1: Organic and Bio-Organic Chemistry (1996), (24),  
 2869-2872  
 CODEN: JCPRB4; ISSN: 0300-922X  
 PUBLISHER: Royal Society of Chemistry  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 126:131656  
 GI



AB Two C-2' hydroxymethyl analogs I of docetaxel have been synthesized from  
 10-deacetyl baccatin III and enantiopure (3S)-3-(N-tert-  
 butoxycarbonylamino)-2-methylene-3-phenylpropanoic acid. The latter was  
 prepared via the use of a new method, the reductive condensation of a chiral  
 propiolate with benzaldehyde imines. I have no significant cytotoxicity  
 vs. KB or KB-V1, but the threo isomer did show more inhibition of  
 microtubule depolymer. than the erythro.

IT 186371-30-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological  
 study); PREP (Preparation)

(asym. Baylis-Hillman-like reaction to prepare  $\alpha$ -aminoalkylacrylic  
 acid derivs. in synthesis of docetaxel hydroxymethyl analogs)

RN 186371-30-2 CAPLUS

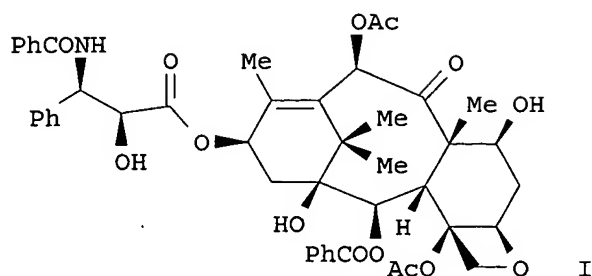
CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-  
 $\alpha$ -hydroxy- $\alpha$ -(hydroxymethyl)-, 12b-(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
 ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ R\*, $\beta$ S  
 \*)],11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PRIORITY APPLN. INFO.:  
GI

JP 1995-93741

19950419



AB An antitumor compound NSC-LSC2 (I) is manufactured by culturing cells originate from *Taxus* sp., recovery of the cultured cells, and collection of I from the cells. New leaves of *T. cuspidata* were cultured in a solid Schenk-Hildebrandt (SH) medium (pH 5.8) containing NAA to 5 mg/L at 20° or 25° under light, subcultured in a liquid modified SH medium (pH 5.8) containing NAA to 5 mg/L, KNO<sub>3</sub>, (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, and KH<sub>2</sub>PO<sub>4</sub>, the cells were dried, homogenized, extracted with MeOH-CH<sub>2</sub>Cl<sub>2</sub> mixture, and the extract was fractionated and subjected to HPLC to purify I. I inhibited KB cells (human carcinoma cell line) with IC<sub>50</sub> of 10 ng/mL.

IT 149197-23-9P, NSC-LSC 2

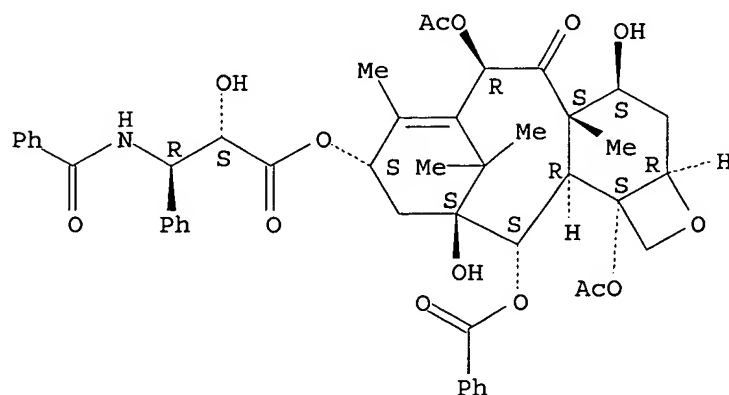
RL: BAC (Biological activity or effector, except adverse); BMF (Bioindustrial manufacture); BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)

(manufacture of antitumor NSC-LSC2 by cell culture of *Taxus*)

RN 149197-23-9 CAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





PRIORITY APPLN. INFO.:

US 1995-523443

A 19950905

AB A process for the separation of taxanes, particularly taxol, cephalomannine, baccatin III, and deacetylbaccatin III, from ornamental yew tissue is described. The process involves a specific solvent mixture of water and 50-95% MeOH, EtOH, or acetone and treatment of the resulting extract using activated C, preferably charcoal. The taxanes are preferably separated from the crude extract by a normal phase chromatog. step which preferably is through vacuum and then medium pressure column chromatog. separation, using inexpensive silica gel as an absorbent. The silica gel is regenerated by heating in a furnace above .apprx.500° to remove adsorbed organic materials.

IT 133577-37-4P

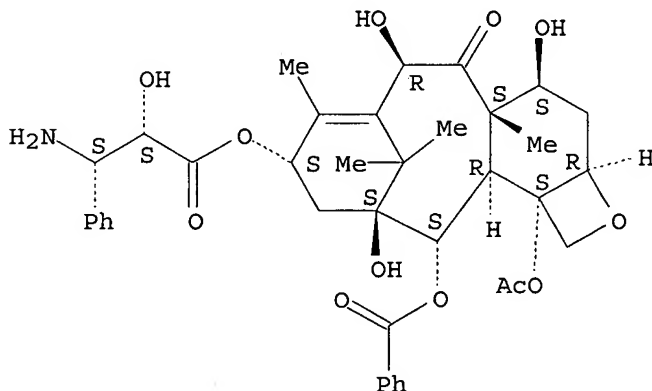
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)

(isolation and purification of taxol and taxanes from Taxus spp.)

RN 133577-37-4 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -amino- $\alpha$ -hydroxy-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*)],11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L51 ANSWER 30 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:72099 CAPLUS

DOCUMENT NUMBER: 126:88340

TITLE: Antitumor compound NSC-LSC2 and its manufacture by cell culture of Taxus

INVENTOR(S): Takigawa, Kenji; Takami, Masamichi; Asari, Tooru; Fukumoto, Kenji

PATENT ASSIGNEE(S): Shinnippon Seitetsu KK, Japan; Shinnittetsu Kagaku

SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08291062	A2	19961105	JP 1995-93741	19950419

discovery through development. This library of paclitaxel degradation derivs. provides a foundation for future development work regarding product monitoring, as well as use as a diagnostic tool for new degradation products.

IT 194148-31-7

RL: ANT (Analyte); ANST (Analytical study)

(determination of paclitaxel degradation derivs. in bulk drug by HPLC and

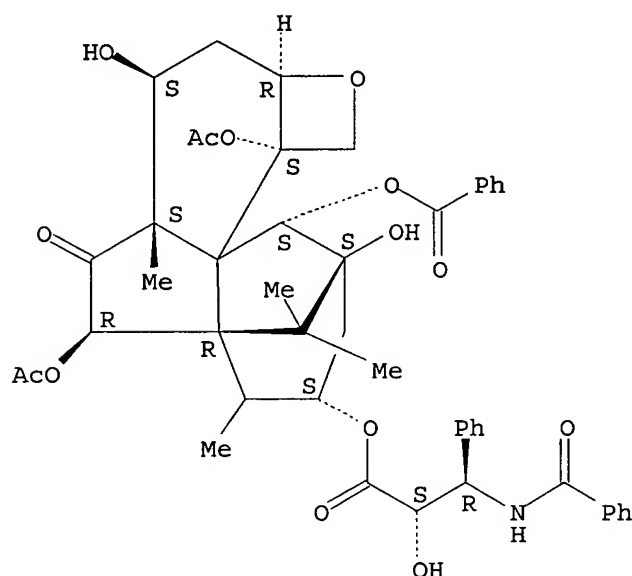
mass

spectrometry)

RN 194148-31-7 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
2a,8-bis(acetyloxy)-3-(benzoyloxy)dodecahydro-4,10-dihydroxy-7,9a,12,12-  
tetramethyl-9-oxo-3H-4,7a-methanocyclohept[3,3a]indeno[5,4-b]oxet-6-yl  
ester, [2aS,3S,4S,6S( $\alpha$ S, $\beta$ R),7aR,8R,9aS,10S,11aR]-[partial]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 29 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:267272 CAPLUS

DOCUMENT NUMBER: 126:255480

TITLE: Process for the isolation and purification of taxol and taxanes from Taxus spp

INVENTOR(S): Nair, Muraleedharan G.

PATENT ASSIGNEE(S): Michigan State University, USA

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

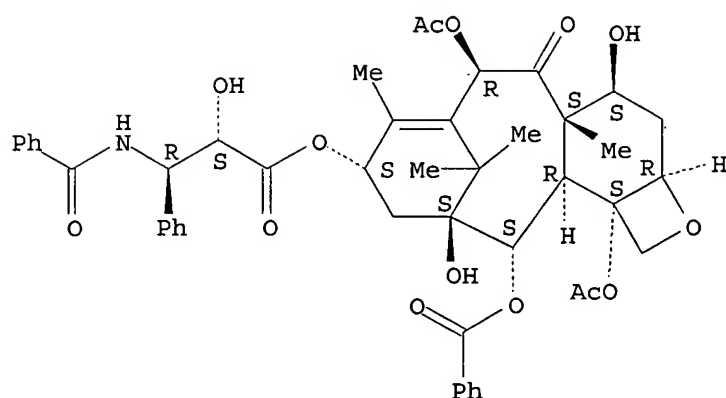
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9709443	A1	19970313	WO 1996-US13212	19960815
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 28 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:469237 CAPLUS

DOCUMENT NUMBER: 127:195561

TITLE: Profiling degradants of paclitaxel using liquid chromatography-mass spectrometry and liquid chromatography-tandem mass spectrometry substructural techniques

AUTHOR(S): Volk, Kevin J.; Hill, Susan E.; Kerns, Edward H.; Lee, Mike S.

CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, P.O. Box, 5100, Wallingford, CT, 06492, USA

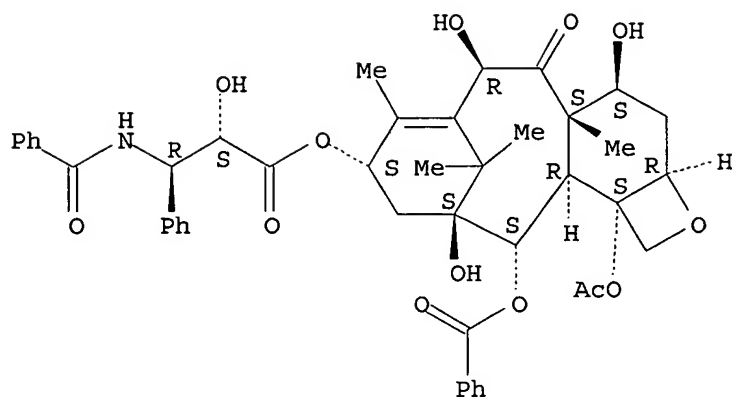
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1997), 696(1), 99-115  
CODEN: JCBEP; ISSN: 0378-4347

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

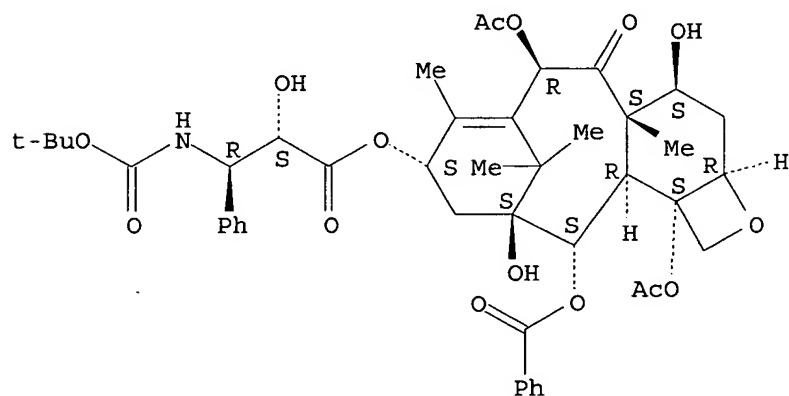
AB A rapid and systematic strategy based on liquid chromatog.-mass spectrometry (LC-MS) profiling and liquid chromatog.-tandem mass spectrometry (LC-MS-MS) substructural techniques was utilized to elucidate the degradation products of paclitaxel, the active ingredient in Taxol. This strategy integrates, in a single instrumental approach, anal. HPLC, UV detection, full-scan electrospray MS, and MS-MS to rapidly and accurately elucidate structures of impurities and degradation derivs.. In these studies, degradation derivs. induced by acid, base, peroxide, and light were profiled using LC-MS and LC-MS-MS methodologies resulting in an LC-MS degradant database which includes information on mol. structures, chromatog. behavior, mol. mass, and MS-MS substructural information. The stressing conditions which may cause drug degradation are utilized to validate the anal. monitoring methods and serve as predictive tools for future formulation and packaging studies. Degradation products formed upon exposure to basic conditions included baccatin III, paclitaxel side chain Me ester, 10-deacetylpaclitaxel, and 7-epipaclitaxel. Degradation products formed upon exposure to acidic conditions included 10-deacetylpaclitaxel and the oxetane ring opened product. Treatment with hydrogen peroxide produced only 10-deacetylpaclitaxel. Exposure to high intensity light produced a number of degradation derivs.. The most abundant photodegradant of paclitaxel corresponded to an isomer which contains a C3-C11 bridge. These methodologies are applicable at any stage of the drug product cycle from



RN 125354-17-8 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 149197-23-9 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

AB Using the method of stepwise multivariate linear regression (SMLR), the quant. structure-activity relationships (QSAR) of two isomeric series of taxol and its derivs. were studied. The molar refractivity of the C3' substituent of the C13 side chain showed significant correlation with its activity. The results suggest that structural changes in the C3' substituents may be critical to the anticancer function.

IT 114977-29-6 125354-13-4 125354-17-8

149197-23-9

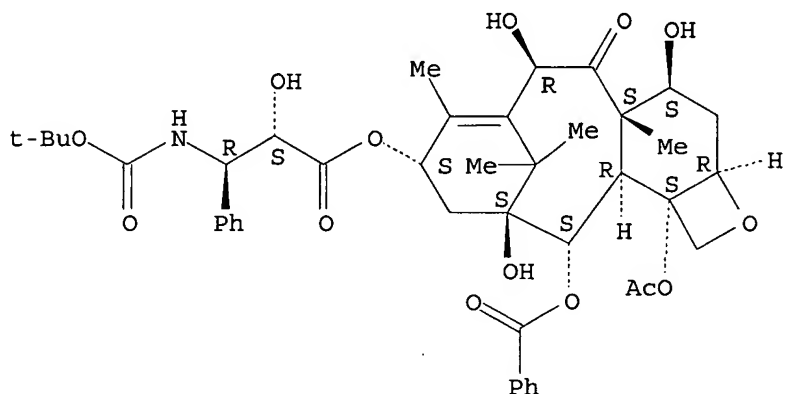
RL: PRP (Properties)

(QSAR of taxol and its derivs. based on stepwise multivariate linear regression anal.)

RN 114977-29-6 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

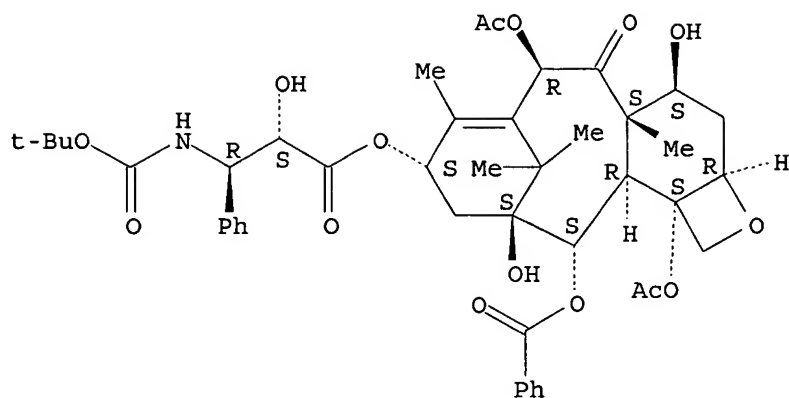
Absolute stereochemistry.



RN 125354-13-4 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

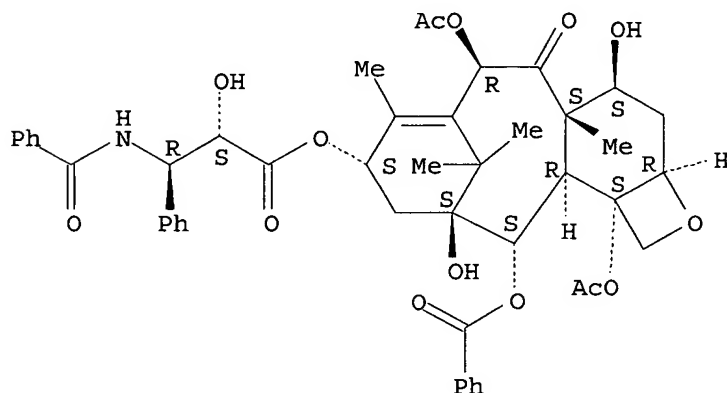
Absolute stereochemistry.



RN 149197-23-9 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, ( $\alpha$ S, $\beta$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 27 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:578023 CAPLUS

DOCUMENT NUMBER: 127:234448

TITLE: Study on QSAR of taxol and its derivatives based on  
stepwise multivariate linear regression analysis

AUTHOR(S): Liu, Ailin; Chi, Hanlin

CORPORATE SOURCE: Inst. Materia Medica, Peking Union Medical College,  
Beijing, 100050, Peop. Rep. China

SOURCE: Journal of Chinese Pharmaceutical Sciences (1997),  
6(1), 18-22

CODEN: JCHSE4; ISSN: 1003-1057

PUBLISHER: Beijing Medical University, School of Pharmaceutical  
Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

TITLE: Comparative Molecular Field Analysis of A Series of  
Paclitaxel Analogs  
AUTHOR(S): Zhu, Qiqing; Guo, Zongru; Huang, Niu; Wang, Minmin;  
Chu, Fengming  
CORPORATE SOURCE: Department of Synthetic Medicinal Chemistry Institute  
of Materia Medica Chinese Academy of Medical Sciences,  
Peking Union Medical College, Beijing, 100050, Peop.  
Rep. China  
SOURCE: Journal of Medicinal Chemistry (1997), 40(26),  
4319-4328  
CODEN: JMCMAR; ISSN: 0022-2623  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A series of 94 paclitaxel analogs exhibiting antitumor activity by promoting the assembly of microtubules and inhibiting the disassembly process of microtubules to tubulin were investigated using the comparative mol. field anal. (CoMFA) method. These compds. belonging to 10 structural classes were randomly divided into a training set of 80 compds. and a test set of 14 compds. Since the 3-dimensional structure of ligand-receptor complex is unknown, from x-ray and NMR data, the authors rationally selected the 3-dimensional structure of paclitaxel in a polar solution as the active conformation and starting structure for mol. modeling, the other mols. were aligned using this mol. model as the template. The most optimal CoMFA yielded a 2-component model, with significant cross-validation  $r^2_{cv}$  of 0.640 and conventional  $r^2$  of 0.868. The predictive ability of training set model was tested on the test set of 14 compds. The tests not only revealed the robustness of the CoMFA model but demonstrated that for this model  $r^2_{pred}$  based on the mean activity of test set compds. can accurately estimate external predictivity but  $r^2_{pred}$  based on the mean activity of training set compds. overestimated the model. The CoMFA model explained why the activity of taxoid is sensitive to the stereochem. of the atoms at C-2' and C-3' positions and the presence of hydroxyl group at C-2' position. The other factors affecting activity were also elucidated according to standard coefficient contour maps of steric

and

electrostatic fields derived from the CoMFA model.

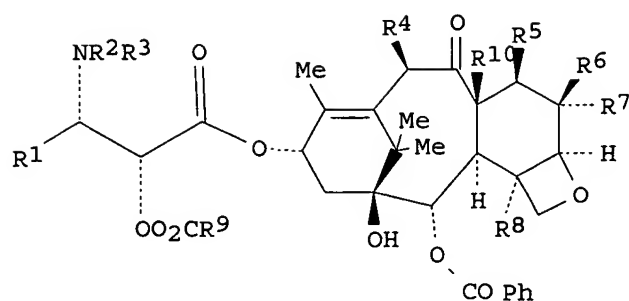
IT 125354-17-8 149197-23-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(comparative mol. field anal. of paclitaxel analogs)

RN 125354-17-8 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



I

AB Taxane derivs. I [R1 = alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl; R2, R3 = H, sulfenamido; R4 = H, OH, Ac; R5 = H, OH, alkoxy, acyloxy, alkoxy-carbonyloxy, carbamoyloxy; R6, R7 = H, OH, alkyl; R5R6 = O, bond, R7 = H; R8 = acyloxy, thioacyloxy; R9 = (un)substituted aryl, cycloalkyl, alkyl, heteroaryl; R10 = Me, CH2OH; R5R10 = CH2] were prepared. The new derivs. are antitumor agents useful in the treatment of such cancers as ovarian, breast, lung, gastric, colon, head and neck, melanoma and leukemia. Thus, I [R1, R9 = Ph, R2, R3, R6, R7 = H, R4, R8 = OAc, R5 = OH, R10 = Me] was treated with 2-O2NC6H4SCl to give I [R2 = 2-O2NC6H4S, other R groups unchanged] which was active against M109 lung carcinoma in mice.

IT 214146-88-0P

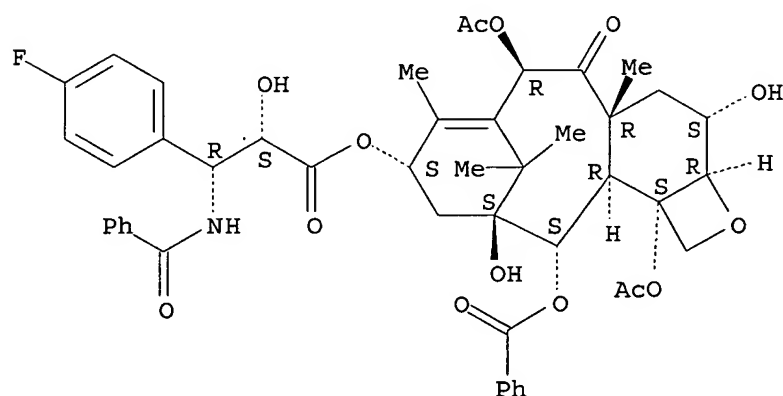
RL: BYP (Byproduct); PREP (Preparation)

(preparation of sulfenamide derivs. of paclitaxel as antitumor agents)

RN 214146-88-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)-4-fluoro- $\alpha$ -hydroxy-, (2aR,3S,4aR,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-3,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

3

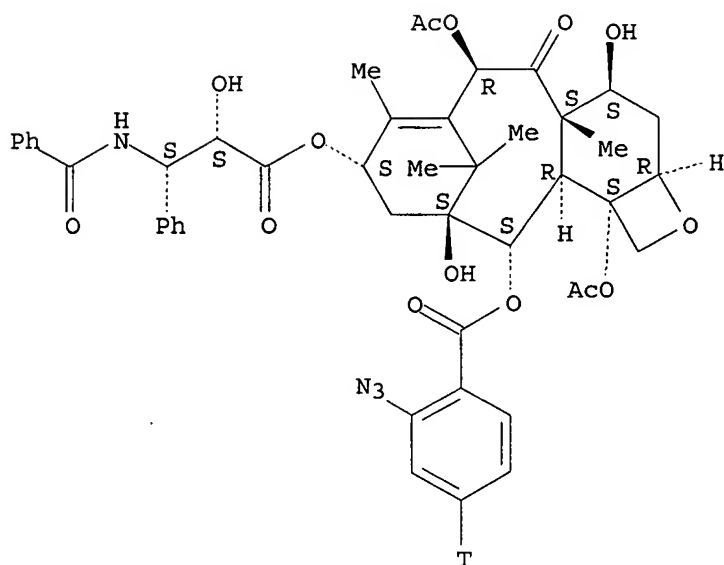
THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 26 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:31653 CAPLUS

DOCUMENT NUMBER: 128:30043

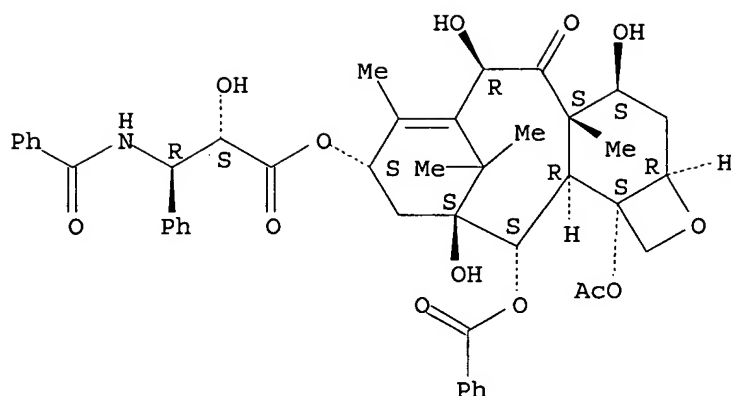




REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 25 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1998:668019 CAPLUS  
DOCUMENT NUMBER: 129:290253  
TITLE: Sulfenamide taxane derivatives  
INVENTOR(S): Scola, Paul M.; Vyas, Dolatrai M.  
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA  
SOURCE: U.S., 29 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5821263	A	19981013	US 1997-902451	19970729
PRIORITY APPLN. INFO.:			US 1997-902451	19970729
OTHER SOURCE(S):	MARPAT	129:290253		
GI				



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 24 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:5360 CAPLUS

DOCUMENT NUMBER: 130:206928

TITLE: Photoaffinity labeling approach to map the taxol-binding site on the microtubule

AUTHOR(S): Orr, George A.; Rao, Srinivasa; Swindell, Charles S.; Kingston, David G. I.; Horwitz, Susan Band

CORPORATE SOURCE: Albert Einstein College of Medicine, Bronx, NY, 10461, USA

SOURCE: Methods in Enzymology (1998), 298 (Molecular Motors and the Cytoskeleton, Part B), 238-252  
CODEN: MENZAU; ISSN: 0076-6879

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Photoaffinity labeling studies of the interaction of taxol with tubulin were done using the taxol analogs with an arylazide substituent attached to either the C-3' of the A ring side chain or the C-2 of the B ring of the taxoid nucleus. Details of the labeling of microtubules with the photoreactive taxol analogs, isolation of  $\beta$ -tubulin and determination of the binding sites on tubulin are outlined. (c) 1998 Academic Press.

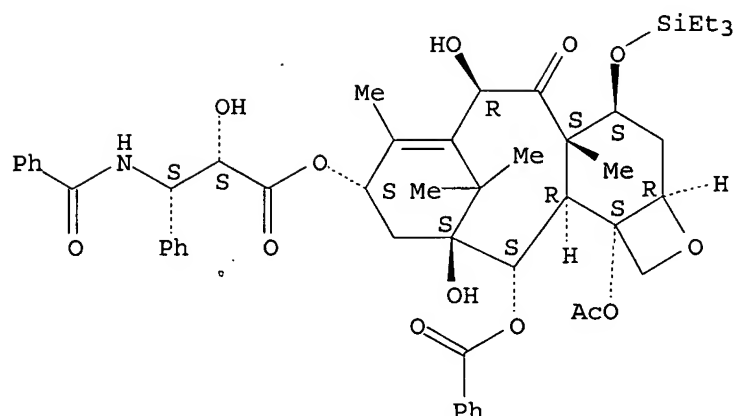
IT 220916-61-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(photoaffinity labeling approach to map the taxol-binding site on the microtubule using arylazide derivs. of taxol)

RN 220916-61-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-[(2-azidobenzoyl-4-t)oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 23 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:322978 CAPLUS

DOCUMENT NUMBER: 131:124926

TITLE: A Unified and Quantitative Receptor Model for the Microtubule Binding of Paclitaxel and Epothilone

AUTHOR(S): Wang, Minmin; Xia, Xiaoyang; Kim, Yohan; Hwang, David; Jansen, Johanna M.; Botta, Maurizio; Liotta, Dennis C.; Snyder, James P.

CORPORATE SOURCE: Department of Chemistry, Emory University, Atlanta, GA, 30322, USA

SOURCE: Organic Letters (1999), 1(1), 43-46

CODEN: ORLEF7; ISSN: 1523-7060

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Paclitaxel and epothilone represent the two major classes of antimicrotubule agents that promote tubulin polymerization and, presumably, mitotic arrest during cell division. A common minireceptor binding site model at  $\beta$ -tubulin has been constructed for these structurally divergent compds. Utilizing 20 amino acids identified in photoaffinity labeling expts., the 3-D model correlates measured and predicted  $K_i$ 's with  $r = 0.99$  and  $\text{rms}(\Delta G_{\text{calc}} - \Delta G_{\text{exp}}) = 0.2 \text{ kcal/mol}$ . In addition, the model predicts the affinity of compds. not used in the training set and explains much of the SAR for the paclitaxel and epothilone families.

IT 125354-13-4

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)

(A Unified and Quant. Receptor Model for the Microtubule Binding of Paclitaxel and Epothilone)

RN 125354-13-4 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

243-246

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 132:194518

AB A semisynthesis of paclitaxel has successfully been accomplished starting from a newly developed baccatin III derivative bearing a  $\beta$ -keto ester appendage on C-13.

IT 260249-50-1P 260261-02-7P

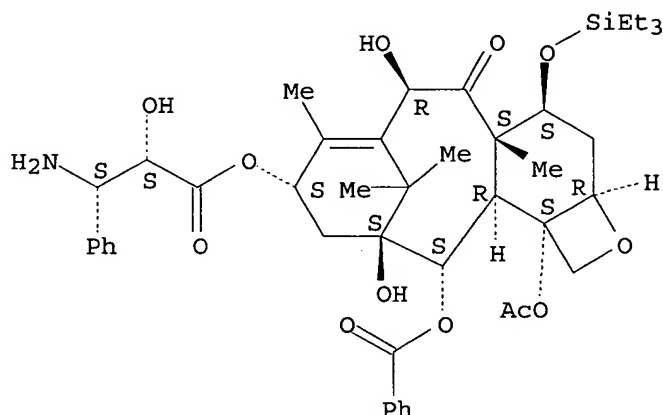
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(semisynthesis of paclitaxel via a 10-deacetylbaccatin III derivative bearing a  $\beta$ -keto ester appendage)

RN 260249-50-1 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -amino- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-6,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 260261-02-7 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-6,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

SOURCE: University, Tianjin, 300072, Peop. Rep. China  
Gaodeng Xuexiao Huaxue Xuebao (2000), 21(3), 401-406  
CODEN: KTHPDM; ISSN: 0251-0790

PUBLISHER: Gaodeng Jiaoyu Chubanshe

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

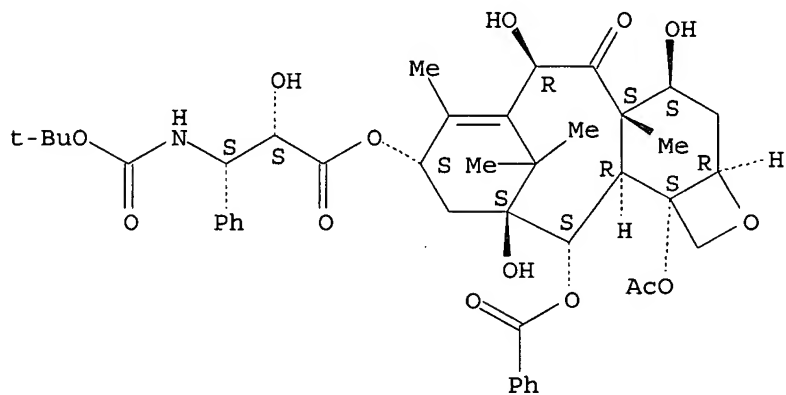
AB A series of 98 paclitaxel analogs were investigated using the comparative mol. field anal. (CoMFA) and a high predictive 3D-QSAR model with a significant cross-validated  $\gamma_{cv2}$ , conventional  $\gamma^2$ , and predictive  $\gamma_{pred.2}$  equaling to 0.714, 0.901, 0.812, resp., was obtained. It revealed that the changes of the C-13 side chain groups, especially 2'-OH, affected the activity significantly and others did less relatively. It also showed that the model was significant for the research and development of novel paclitaxel analogs to reduce the blind flight during drug designing.

IT 133577-33-0  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(studies on the quant. structure-activity relationships of paclitaxel analogs)

RN 133577-33-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 22 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:42193 CAPLUS

DOCUMENT NUMBER: 132:194518

TITLE: A semisynthesis of paclitaxel via a 10-deacetylbaccatin III derivative bearing a  $\beta$ -keto ester appendage

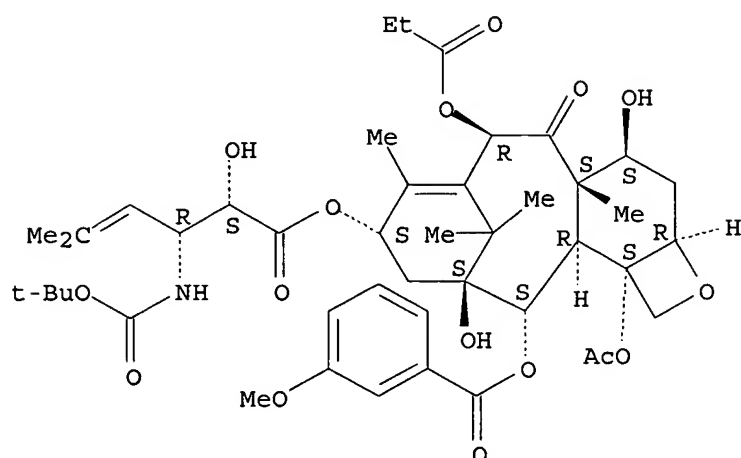
AUTHOR(S): Mandai, Tadakatsu; Kuroda, Akiyoshi; Okumoto, Hiroshi; Nakanishi, Katsuyoshi; Mikuni, Katsuhiko; Ko-Ji, Hara; Ko-Zo, Hara

CORPORATE SOURCE: Department of Chemical Technology, Kurashiki University of Science and the Arts, Kurashiki, 712-8505, Japan

SOURCE: Tetrahedron Letters (1999), Volume Date 2000, 41(2),

1H-cyclodeca[3,4]benz[1,2-b]oxet-12-yl ester (9CI) (CA INDEX NAME)

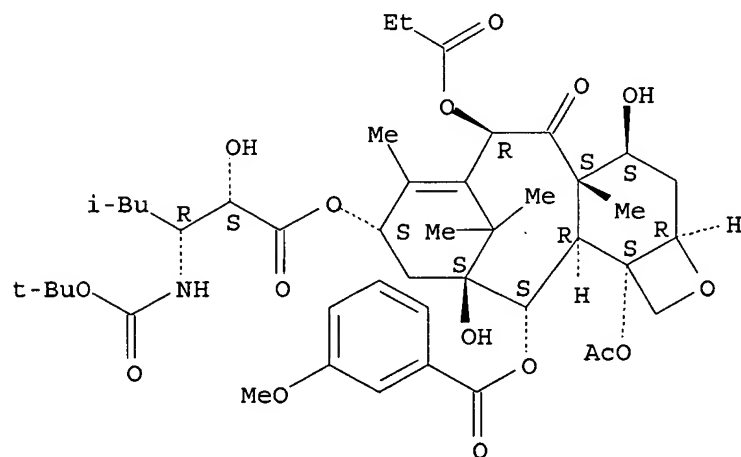
Absolute stereochemistry.



RN 287180-37-4 CAPLUS

CN Benzoic acid, 3-methoxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-9-[[[(2S,3R)-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-1-oxohexyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-6-(1-oxopropoxy)-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-12-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 21 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:218668 CAPLUS

DOCUMENT NUMBER: 133:255

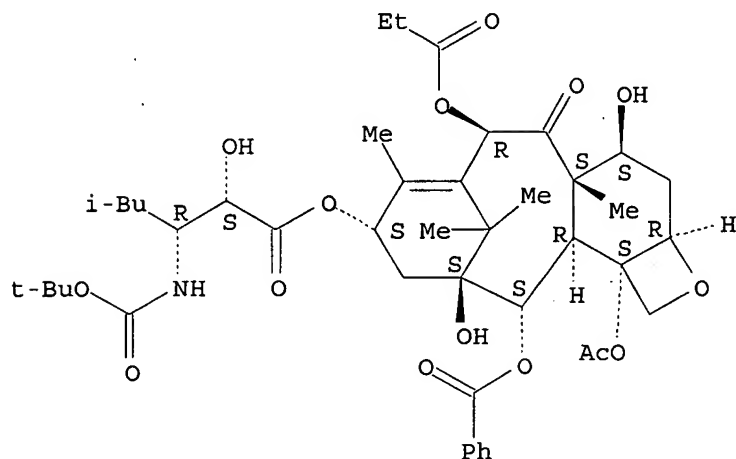
TITLE: Studies on the quantitative structure-activity relationships of paclitaxel analogs

AUTHOR(S): Shi, Bing-Xing; Liang, Shi-Le; Yuan, Ying-Jin; Sun, Ming; Miao, Fang-Ming

CORPORATE SOURCE: Department of Biochemical Engineering, Tianjin

2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-6-(1-oxopropoxy)-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2S,3R)- (9CI) (CA INDEX NAME)

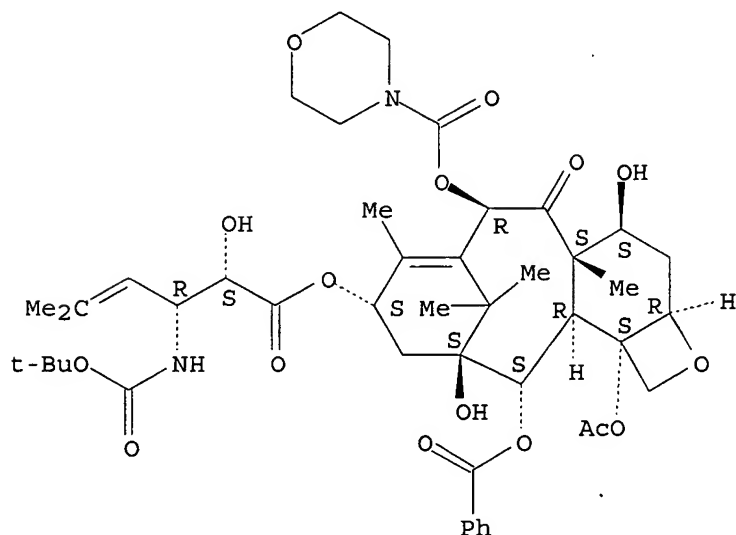
Absolute stereochemistry.



RN 287180-35-2 CAPLUS

CN 4-Morpholinecarboxylic acid, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-9-[[[(2S,3R)-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-1-oxo-4-hexenyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-6-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 287180-36-3 CAPLUS

CN Benzoic acid, 3-methoxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-9-[[[(2S,3R)-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-1-oxo-4-hexenyl]oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-6-(1-oxopropoxy)-7,11-methano-

CORPORATE SOURCE: Rutter, Jessica; Ojima, Iwao  
 SOURCE: Department of Chemistry, State University of New York  
 at Stony Brook, Stony Brook, NY, 11794-3400, USA  
 Chirality (2000), 12(5/6), 431-441  
 CODEN: CHRLEP; ISSN: 0899-0042  
 PUBLISHER: Wiley-Liss, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 133:150742

AB A series of highly potent second-generation taxoids bearing a 2-methylprop-1-enyl or a 2-methylpropyl group at C-3' with modifications at the C-2, C-10, and C-14 positions was synthesized through the coupling of racemic cis- $\beta$ -lactams with properly protected/modified baccatin and 14-OH-baccatin. A high level of kinetic resolution was observed for all cases examined. The observed highly efficient enantiomer differentiation is ascribed to the markedly different chiral environment between the (+)- and (-)- $\beta$ -lactams in their approach to the chiral framework of the enantiopure lithium alkoxide of a baccatin in the ring-opening coupling process. It was also observed that substantially higher selectivity was achieved when 14-OH-baccatin-1,14-carbonate was used. Anal. of the transition state models revealed that the repulsive interactions between the 3-TIPS group of a (-)- $\beta$ -lactam with 1,14-carbonate group of the baccatin substantially increases the asym. bias in the kinetic resolution process, favoring the reaction of a (+)- $\beta$ -lactam, which leads to the observed excellent selectivity.

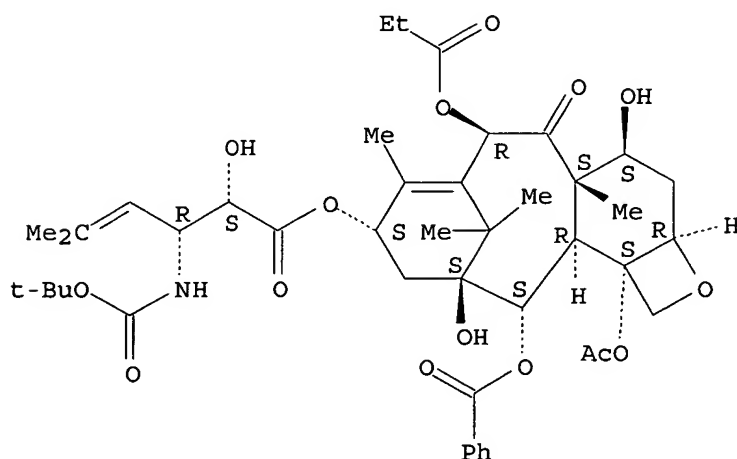
IT 287180-33-0P 287180-34-1P 287180-35-2P  
 287180-36-3P 287180-37-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of highly potent second-generation taxoids through effective kinetic resolution coupling of racemic  $\beta$ -lactams with baccatins)

RN 287180-33-0 CAPLUS

CN 4-Hexenoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-6-(1-oxopropoxy)-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2S,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



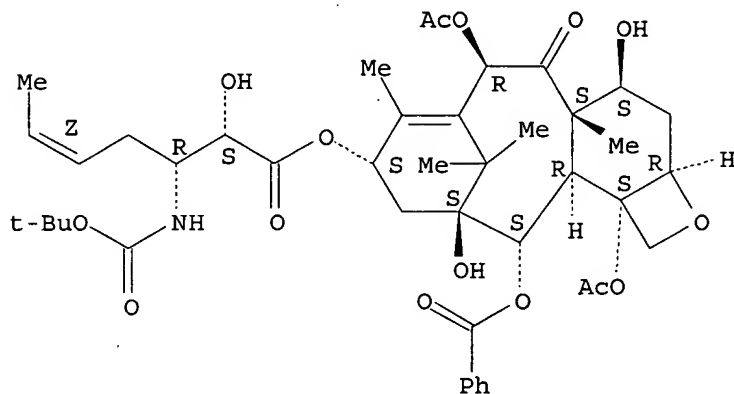
RN 287180-34-1 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-



(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2S,3R,5Z)- (9CI) (CA INDEX NAME)

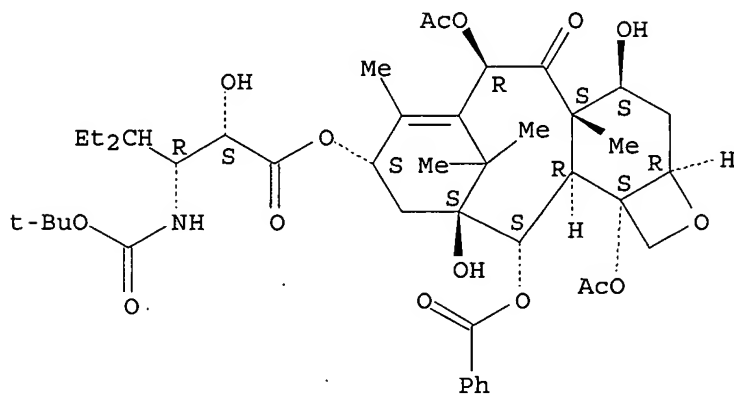
Absolute stereochemistry.  
Double bond geometry as shown.



RN 292608-64-1 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy) carbonyl] amino]-4-ethyl-2-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2S,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 20 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:374253 CAPLUS

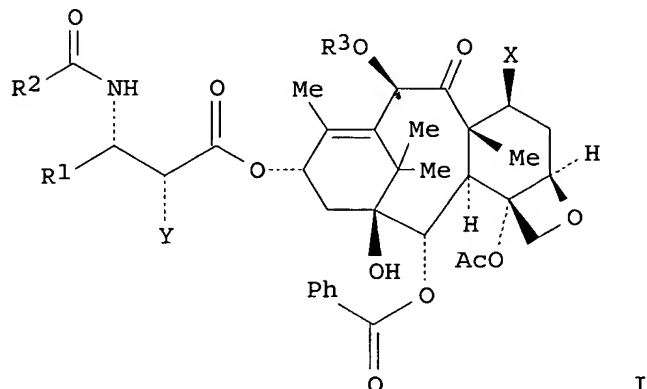
DOCUMENT NUMBER: 133:150742

TITLE: Synthesis of highly potent second-generation taxoids through effective kinetic resolution coupling of racemic  $\beta$ -lactams with baccatins

AUTHOR(S): Lin, Songnian; Geng, Xudong; Qu, Chuanxing; Tynebor, Robert; Gallagher, David J.; Pollina, Elizabeth;

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053592	A1	20000914	WO 2000-JP1334	20000306
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2003026673	A2	20030129	JP 1999-59415	19990305
PRIORITY APPLN. INFO.:			JP 1999-59415	A 19990305
OTHER SOURCE(S):	MARPAT 133:238151			
GI				



I

AB Claimed are osteogenesis promoters containing taxoids represented by general formula (I) in amts. effective for osteogenesis (wherein X and Y are each independently hydroxyl or a group convertible into hydroxyl in vivo; R1 is alkyl, alkenyl, alkynyl, Ph, naphthyl, furyl, or thienyl; R2 is alkyl, Ph, naphthyl, furyl, thienyl, alkoxy, or alkylamino; and R3 is hydrogen, alkyl, alkylcarbonyl, benzoyl, naphthoyl, furoyl, thenoyl, alkoxy carbonyl, or dialkylcarbonyl) for the treatment of bone fracture and bone loss due to surgical bone removal. Thus, de-N-benzoyl-3'-desphenyl-3'-isobutylpaclitaxel (preparation given) was acylated by di-tert-amyl dicarbonate in a mixture of EtOAc and saturated aqueous NaHCO<sub>3</sub> at room temperature for 5 h to give

de-N-benzoyl-N-tert-amylloxycarbonyl-3'-desphenyl-3'-isobutylpaclitaxel (II). II in vitro increased number of bone nodules formed in rat osteoblastic cell from 5.3±5.2 (control) to 25, 64, and 97/well at 0.3, 1, and 4 ng/mL, resp.

IT 292608-56-1P 292608-64-1P

RL: BYP (Byproduct); PREP (Preparation)

(preparation of taxoid compds. as osteogenesis promoters for treatment of bone fracture and bone loss due to surgical bone removal)

RN 292608-56-1 CAPLUS

CN 5-Heptenoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-,

CORPORATE SOURCE: Miao, Fang-ming  
School of Chemical Engineering, Tianjin University,  
Tianjin, 300072, Peop. Rep. China

SOURCE: Tianjin Daxue Xuebao, Ziran Kexue Yu Gongcheng  
Jishuban (2000), 33(1), 51-55  
CODEN: TDXZAE

PUBLISHER: Tianjin Daxue Xuebao Bianjibu

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

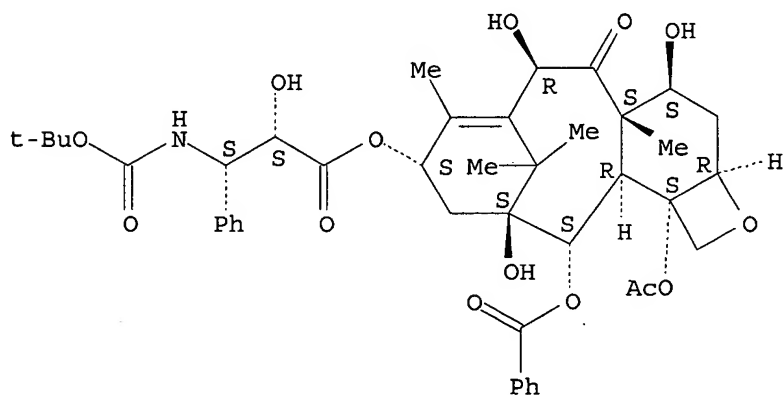
AB A series of 58 paclitaxel analogs with different pharmacophores have been investigated using the comparative mol. field anal. (CoMFA), and a 3D-quant. structure-activity relationship (3D-QSAR) model with high prediction has been obtained. The model is very significant for the research and development of novel paclitaxel analogs and decreasing the blindness in drug design.

IT 133577-33-0  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(development and application of 3D-quant. structure-activity relationship model of paclitaxel analogs)

RN 133577-33-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 19 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:646001 CAPLUS

DOCUMENT NUMBER: 133:238151

TITLE: Preparation of taxoid compounds as osteogenesis promoters

INVENTOR(S): Ishizuya, Toshinori; Ikuta, Shunichi; Uzawa, Toyonobu; Hori, Masayuki

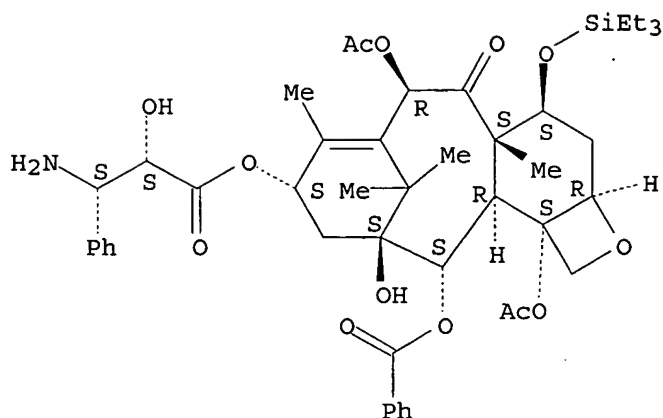
PATENT ASSIGNEE(S): Asahi Kasei Kogyo Kabushiki Kaisha, Japan

SOURCE: PCT Int. Appl., 152 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1



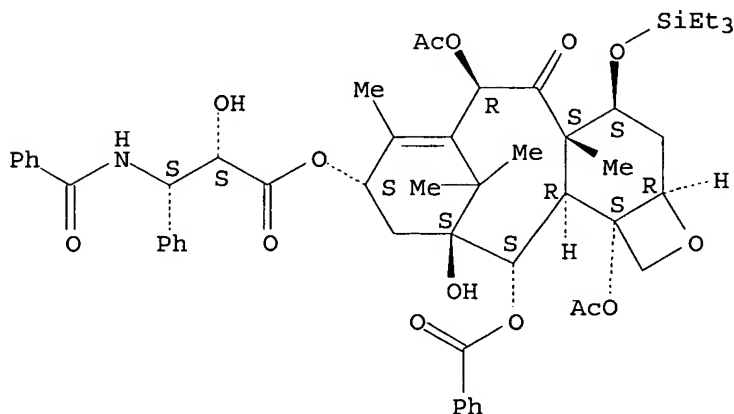
IT 301835-15-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of taxoid compds.)

RN 301835-15-4 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 18 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:704912 CAPLUS

DOCUMENT NUMBER: 134:187814

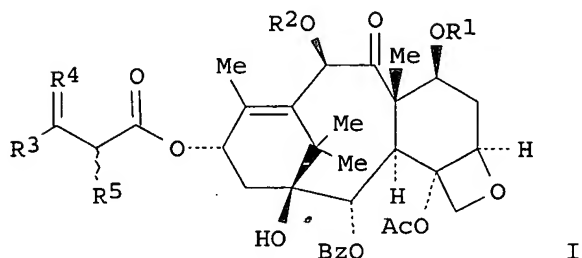
TITLE: Development and application of 3D-quantitative structure-activity relationship model of paclitaxel analogs

AUTHOR(S): Liu, Bin; Shi, Bing-xing; Yuan, Ying-jin; Sun, Ming;

IE, SI, LT, LV, FI, RO  
 PRIORITY APPLN. INFO.:  
 OTHER SOURCE(S): MARPAT 133:310031  
 GI

JP 1999-263974

A 19990917



AB A method for the preparation of taxoid compds. (I) [R1, R2 = hydroxy protecting group; R3 = aryl, heteroaryl, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl etc.; R4 = NOR6 ; R5 = OH; R6 = CH2Ph, Me, Et, CPh, COMe] was developed. Thus, I [R1 = TES, R2 = BOC, R3 = Ph, R4 = N-OBn, R5 =  $\alpha$ -OH (II)] was prepared by oximation with O-benzylhydroxylamine hydrochloride of protected 10-deacetylbaccatin III, followed by azotization with tosyl azide, reaction with copper acetylacetonate and deacetylation of acetoxyoxime in presence of 1-chloro-3-hydroxytetraethylsiloxane. Methods for producing the taxoid derivative I (R4 = O) from a baccatin derivative and other taxoid compds. such as paclitaxel from I (R4 = O) through intermediate compds. (amino-alc., benzoylamino-alc. and oxazoline) are also disclosed.

IT 301835-14-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of taxoid compds.)

RN 301835-14-3 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -amino- $\alpha$ -hydroxy-,  
 (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-  
 cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.

and paclitaxel (III) simultaneously or when III preceded II·HCl.

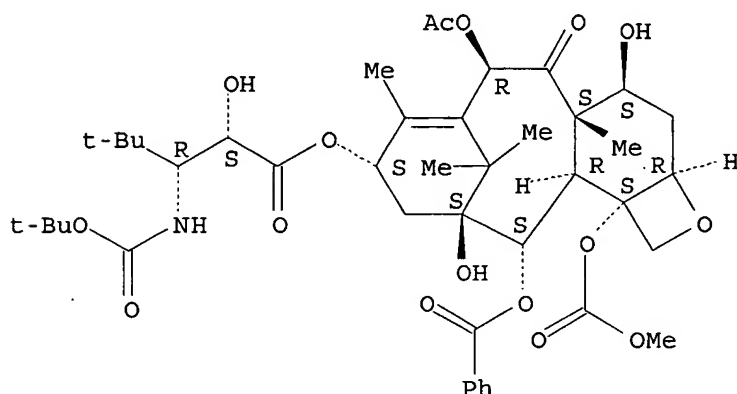
IT 364357-78-8P

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(synergistic methods using two or more anticancer agents for treating cancer)

RN 364357-78-8 CAPLUS

CN D-threo-Pentonic acid, 3,4,5-trideoxy-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-4,4-dimethyl-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-12b-[(methoxycarbonyl)oxy]-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 17 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:752143 CAPLUS

DOCUMENT NUMBER: 133:310031

TITLE: methods for preparation of taxoid compounds from baccatin derivatives

INVENTOR(S): Mandai, Tadakatsu; Okumoto, Hiroshi; Nakanishi, Katsuyoshi; Hara, Koji; Mikuni, Katsuhiko; Hara, Kozo  
PATENT ASSIGNEE(S): Bio Research Corporation of Yokohama, Japan; Ensui Sugar Refining Co., Ltd.

SOURCE: U.S., 19 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent  
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6136990	A	20001024	US 2000-504788	20000215
JP 2001089464	A2	20010403	JP 1999-263974	19990917
AU 724835	B1	20000928	AU 2000-17557	20000217
CA 2299967	AA	20010317	CA 2000-2299967	20000229
CA 2299967	C	20050419		
EP 1085018	A1	20010321	EP 2000-103473	20000301

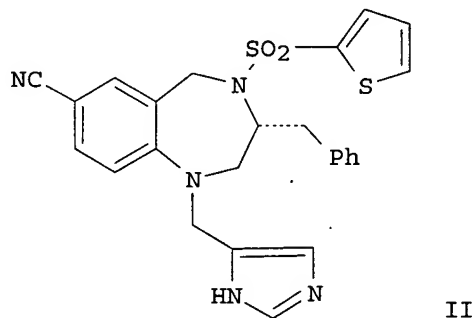
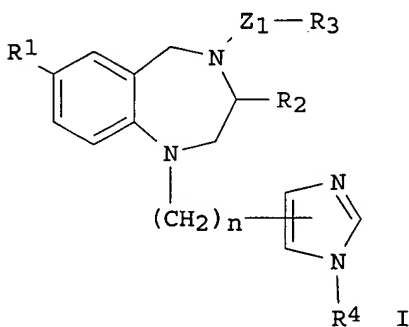
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072721	A2	20011004	WO 2001-US9193	20010322
WO 2001072721	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2404712	AA	20011004	CA 2001-2404712	20010322
EP 1272193	A2	20030108	EP 2001-920653	20010322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003528864	T2	20030930	JP 2001-570634	20010322
RU 2264217	C2	20051120	RU 2002-129000	20010322
BR 2001009517	A	20060829	BR 2001-9517	20010322
US 2002002162	A1	20020103	US 2001-817456	20010326
US 6537988	B2	20030325		
NO 2002004610	A	20021125	NO 2002-4610	20020926
ZA 2002007766	A	20030120	ZA 2002-7766	20020926
PRIORITY APPLN. INFO.:			US 2000-192278P	P 20000327
			WO 2001-US9193	W 20010322

OTHER SOURCE(S): MARPAT 135:288636

GI



AB The present invention provides a synergistic method for the treatment of cancer which comprises administering a synergistically, therapeutically effective amount of: (i) at least agent selected from the group consisting of cytotoxic agents and cytostatic agents, and (ii) a compound of formula [I; R1 = Cl, Br, CN, substituted Ph, substituted pyridyl; R2 = alkyl, aralkyl; R3, R5 = substituted alkyl, aryl, heterocycle; R4 = H, alkyl; Z1 = CO, SO2, CO2, SO2N(R5); n = 1,2] or a pharmaceutically acceptable salt thereof. The present invention further provides a pharmaceutical composition for the synergistic treatment of cancer which comprises at least one agent selected from the group consisting of antiproliferative cytotoxic agents and antiproliferative cytostatic agents, a compound of formula I, and a pharmaceutically acceptable carrier. Synergism was observed when non-proliferating tumor cells were treated with diazepam II·HCl

(3), 97-102

CODEN: HSDZER; ISSN: 1000-5463

PUBLISHER:

Huanan Shifan Daxue

DOCUMENT TYPE:

Journal

LANGUAGE:

Chinese

AB To analyze the QSAR of 13 paclitaxel analogs (for R6 = H), the MM3 geometry optimization and MNDO quantum chemical indexes have been performed. It is concluded that the change of R2 group, the sum of net charge of carbon and oxygen atoms of Bz in 2-O Bz  $\Sigma$  Q Bz, and the energy of core-core interaction Ep, affect the activity significantly. A significant quant. relationship between electronic structure and antimitotic activity of paclitaxel analogs was obtained as follows: ID50(A)/ID50(T)(act) = 71.20535+155.35016  $\Sigma$  QBz. The QSAR reveals that the values of ID50(A)/ID50(T)(act) are decreased, and the activities are increased as the decrease of  $\Sigma$  Q Bz. The superior predictions were obtained, by neural network in the research.

IT 133577-33-0

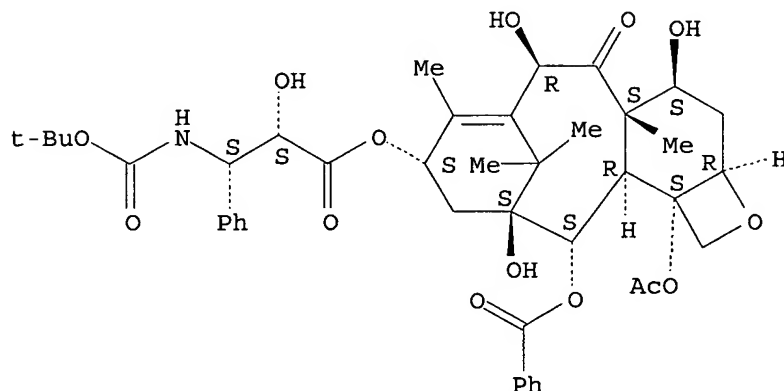
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)

(study on the relationships between the electronic structure and antimitotic activity of paclitaxel analogs)

RN 133577-33-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 16 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:730715 CAPLUS

DOCUMENT NUMBER: 135:288636

TITLE: Synergistic methods and compositions for treating cancer using two or more anticancer agents

INVENTOR(S): Lee, Francis Y.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

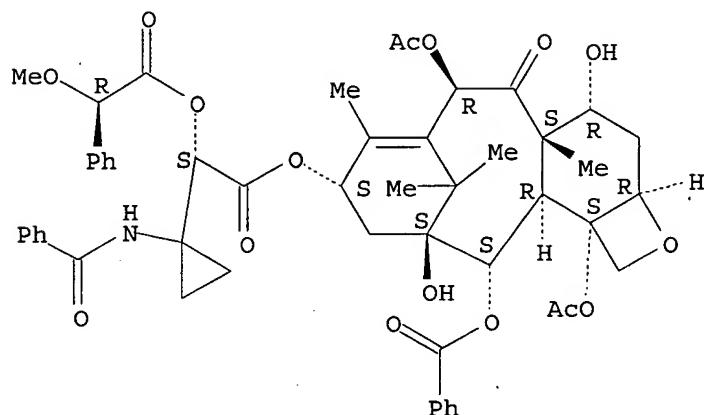
English

FAMILY ACC. NUM. COUNT: 1



9-yl]oxy]-2-oxoethyl ester, ( $\alpha$ R)- (9CI) (CA INDEX NAME)

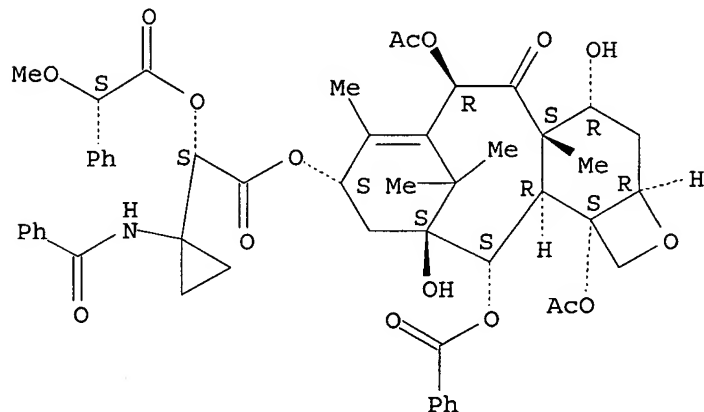
Absolute stereochemistry.



RN 534572-30-0 CAPLUS

CN Benzeneacetic acid,  $\alpha$ -methoxy-, (1S)-1-[1-(benzoylamino)cyclopropyl]-2-[[[(2aR,4R,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl]oxy]-2-oxoethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 15 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:824014 CAPLUS

DOCUMENT NUMBER: 137:27784

TITLE: Study on the relationships between the electronic structure and antimitotic activity of paclitaxel analogs. (I)

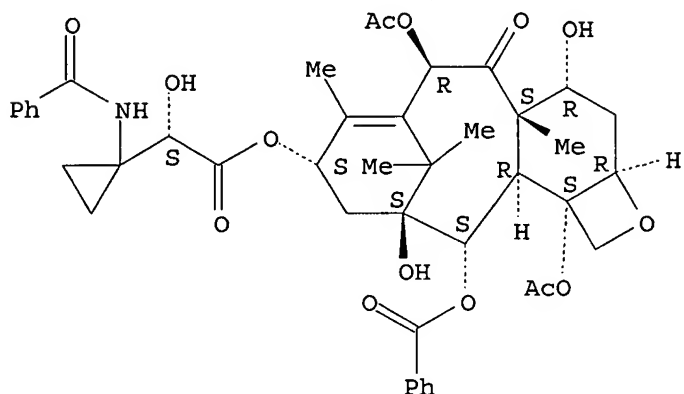
AUTHOR(S): Xu, Zhi-guang; Xu, Xuan; Luo, Yi-fan; Li, Wei-hua

CORPORATE SOURCE: Dep. Chem., South China Normal Univ., Canton, 510631, Peop. Rep. China

SOURCE: Huanan Shifan Daxue Xuebao, Ziran Kexueban (2001),

ester, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 534572-19-5P

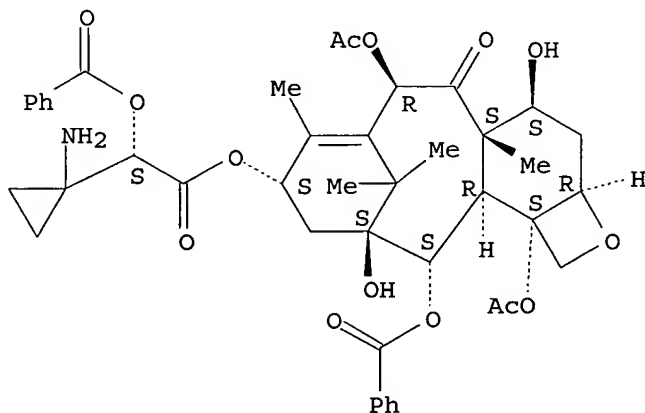
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and anti-cancer activity of paclitaxel analogs with a cyclopropanated side-chain)

RN 534572-19-5 CAPLUS

CN Cyclopropaneacetic acid, 1-amino- $\alpha$ -(benzoyloxy)-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 534572-29-7P 534572-30-0P

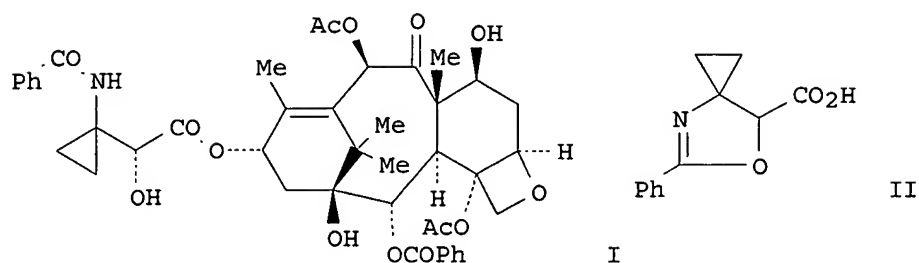
RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis and anti-cancer activity of paclitaxel analogs with a cyclopropanated side-chain)

RN 534572-29-7 CAPLUS

CN Benzeneacetic acid,  $\alpha$ -methoxy-, (1S)-1-[1-(benzoylamino)cyclopropyl]-2-[[[(2aR,4R,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-

LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 139:7034  
 GI



AB Four paclitaxel analogs, such as I, with a cyclopropanated side-chain were synthesized by coupling of the spirocyclopropanated oxazoline-5-carboxylic acid II with 7-O-(triethylsilyl)baccatin III, followed by hydrolytic ring opening and rearrangement. The absolute configuration of the 2'-position was determined by NMR anal. of the corresponding Mosher esters. The two new paclitaxel analogs with the R configuration at C-2' were both active in the A2780 mammalian cell line cytotoxicity assay, but much less than paclitaxel itself.

IT 534572-23-1P 534572-25-3P

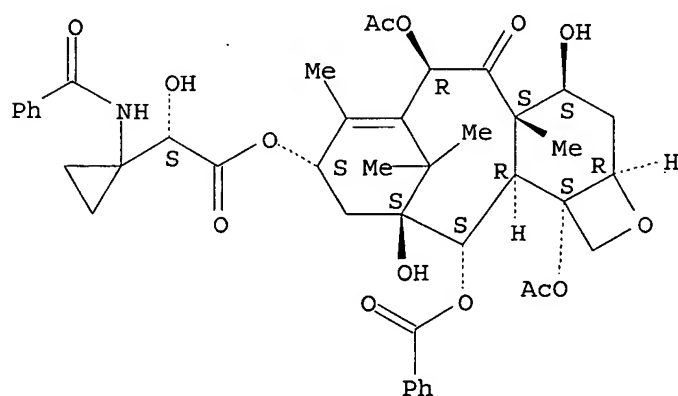
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and anti-cancer activity of paclitaxel analogs with a cyclopropanated side-chain)

RN 534572-23-1 CAPLUS

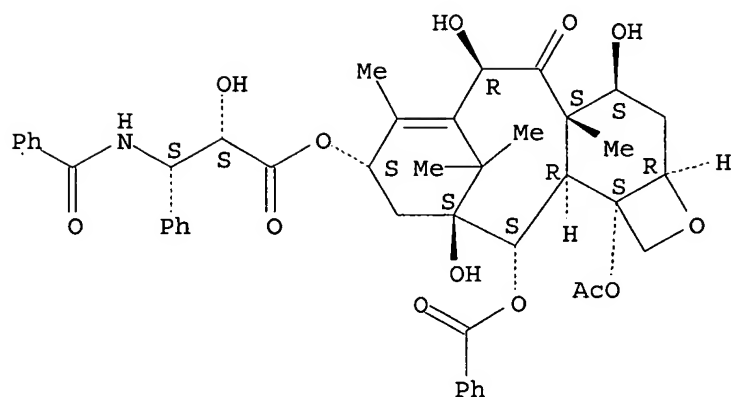
CN Cyclopropaneacetic acid, 1-(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



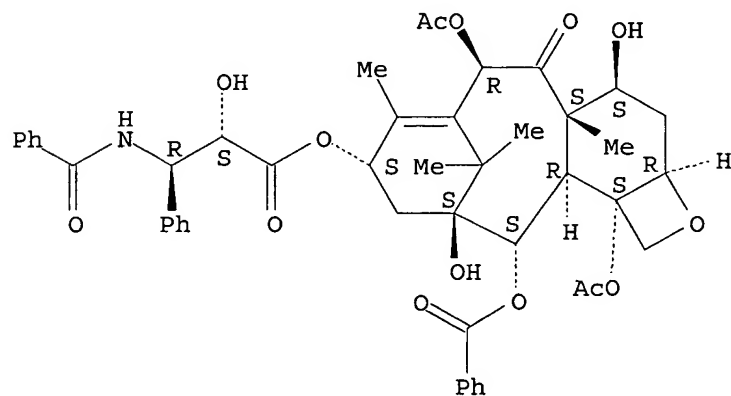
RN 534572-25-3 CAPLUS

CN Cyclopropaneacetic acid, 1-(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4R,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl



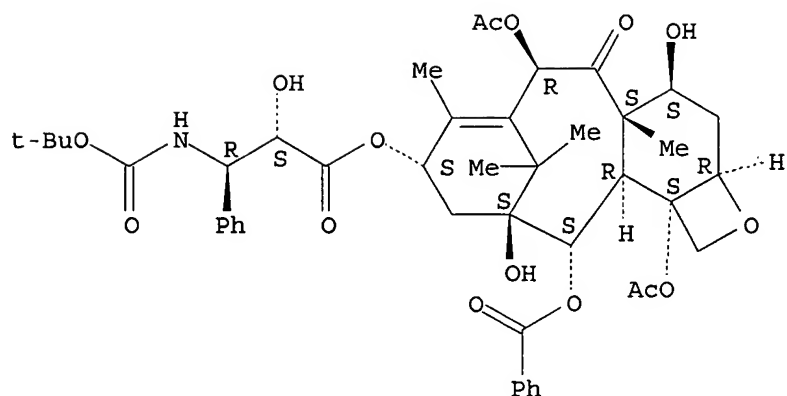
RN 149197-23-9 CAPLUS  
 CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
 (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
 ester, ( $\alpha$ S, $\beta$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

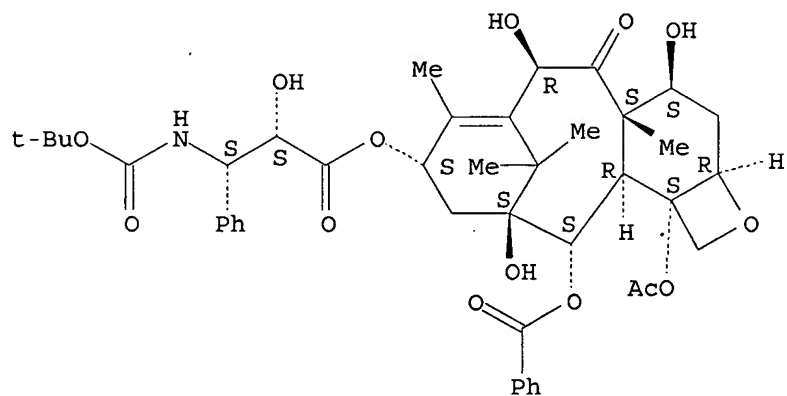
L51 ANSWER 14 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2003:128638 CAPLUS  
 DOCUMENT NUMBER: 139:7034  
 TITLE: Synthesis and bioactivities of paclitaxel analogs with  
 a cyclopropanated side-chain  
 AUTHOR(S): Liu, Changhui; Tamm, Markus; Notzel, Marcus W.; de  
 Meijere, Armin; Schilling, Jennifer K.; Kingston,  
 David G. I.  
 CORPORATE SOURCE: Department of Chemistry, Virginia Polytechnic  
 Institute and State University, Blacksburg, VA, 24061,  
 USA  
 SOURCE: Tetrahedron Letters (2003), 44(10), 2049-2052  
 CODEN: TELEAY; ISSN: 0040-4039  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal



RN 133577-33-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



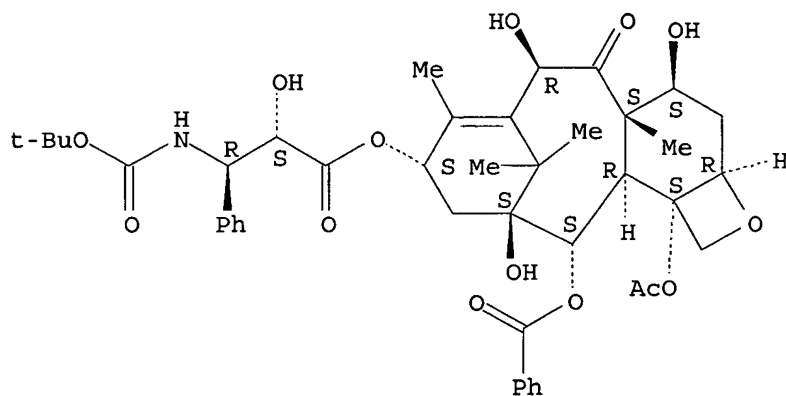
RN 133577-35-2 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)-(9CI) (CA INDEX NAME)

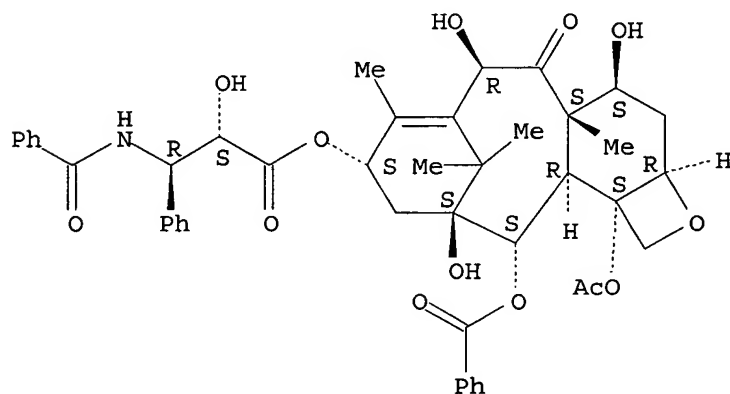
Absolute stereochemistry.



RN 125354-13-4 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

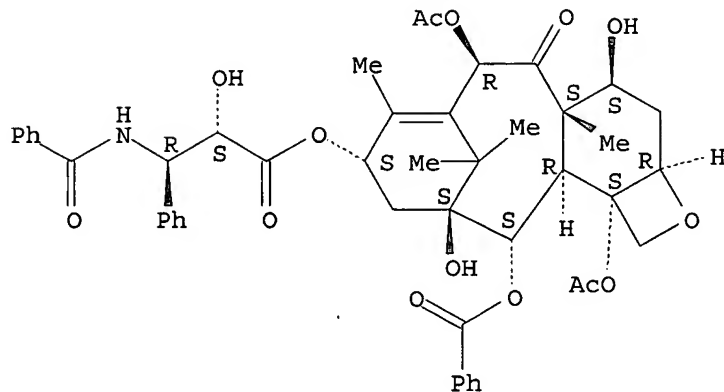


RN 125354-17-8 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 13 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:151052 CAPLUS

DOCUMENT NUMBER: 138:331208

TITLE: A Structure-Activity Study of Taxol, Taxotere, and Derivatives Using the Electronic Indices Methodology (EIM)

AUTHOR(S): Braga, S. F.; Galvao, D. S.

CORPORATE SOURCE: Instituto de Fisica Gleb Wataghin, Universidade Estadual de Campinas, Campinas, 13083-970, Brazil

SOURCE: Journal of Chemical Information and Computer Sciences (2003), 43(2), 699-706

CODEN: JCISD8; ISSN: 0095-2338

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Among the new families of effective anticancer drugs, the natural product paclitaxel (Taxol/Bristol-Myers-Squibb) and its semisynthetic derivative docetaxel (Taxotere/Rhone-Poulenc Rorer) are probably the most promising agents under investigation. Surprisingly considering their importance no detailed quantum mech. studies have been carried out for these drugs. In this work we report the first structure-activity relation (SAR) studies for 20 taxoid structures using mol. descriptors from all-electron quantum methods. The used methods were the pattern-recognition Principal Component Anal. (PCA), Hierarchical Clustering Anal. (HCA), and the recently developed Electronic Indexes Methodol. (EIM). The combined use of EIM with PCA/HCA methodologies was able to correctly classify active and inactive taxoids with 100% of accuracy using only a few "universal" quantum mol. descriptors. It was possible to identify the electronic features defining active mols. This information can be used to select and design new active compds. The combined use of EIM with PCA/HCA can be a new and very efficient tool in the field of computer assisted drug design.

IT 114977-29-6 125354-13-4 125354-17-8

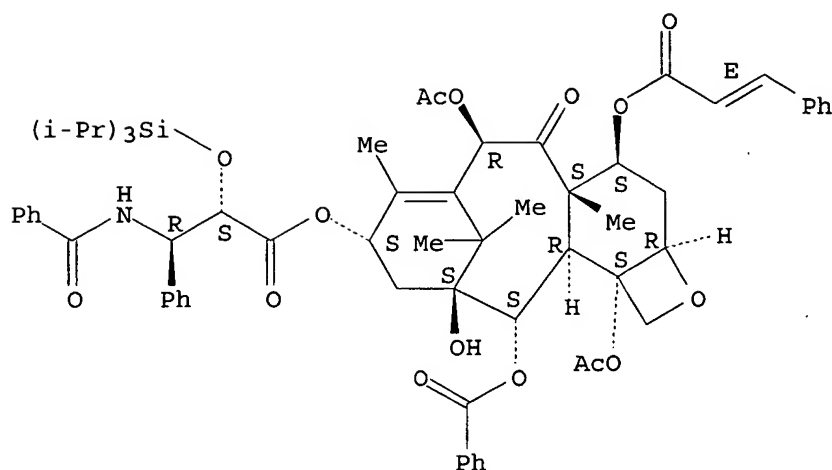
133577-33-0 133577-35-2 149197-23-9

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(structure-activity study of Taxol, Taxotere, and derivs. using the electronic indexes methodol.)

RN 114977-29-6 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 12 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:326401 CAPLUS

DOCUMENT NUMBER: 140:35302

TITLE: 3D QSAR studies of the interaction between  $\beta$ -tubulin and microtubule stabilizing antimitotic agents (MSAA). A combined pharmacophore generation and pseudoreceptor modeling approach applied to taxanes and epothilones

AUTHOR(S): Manetti, Fabrizio; Forli, Stefano; Maccari, Laura; Corelli, Federico; Botta, Maurizio

CORPORATE SOURCE: Dipartimento Farmaco Chimico Tecnologico, Universita degli Studi di Siena, Siena, I-53100, Italy

SOURCE: Farmaco (2003), 58(5), 357-361

CODEN: FRMCE8; ISSN: 0014-827X

PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Based on the conformer of paclitaxel extracted from the exptl. tubulin structure, a pharmacophoric model has been generated and used to find the chemical features common to the taxane and epothilone classes of compds. This original alignment has been translated into the exptl. tubulin binding site obtaining an assembly subsequently submitted to the pseudoreceptor modeling approach. As a result, an original 3D QSAR model, able to evaluate, at a quant. level, the relationships between the mol. structures and biol. data of the studied compds., has been obtained.

IT 149197-23-9

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

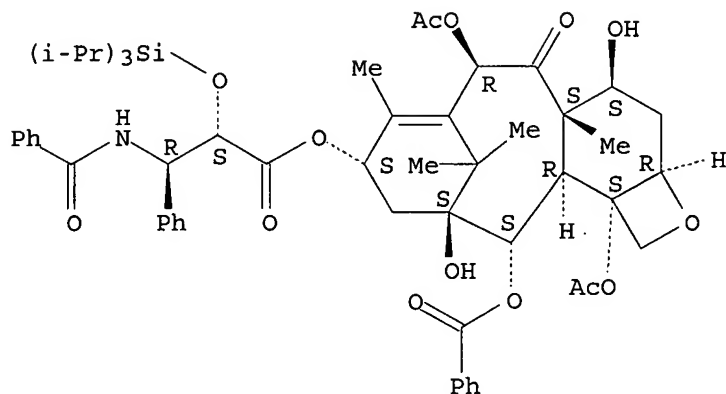
(QSAR studies of the interaction between  $\beta$ -tubulin and microtubule stabilizing antimitotic agents)

RN 149197-23-9 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

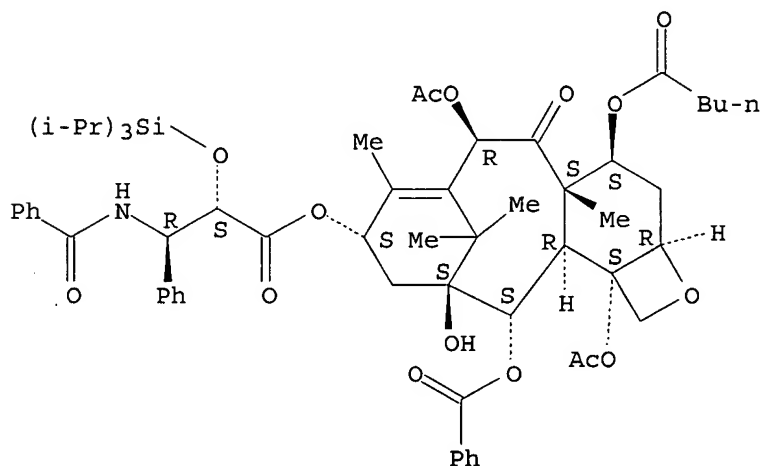


Absolute stereochemistry.



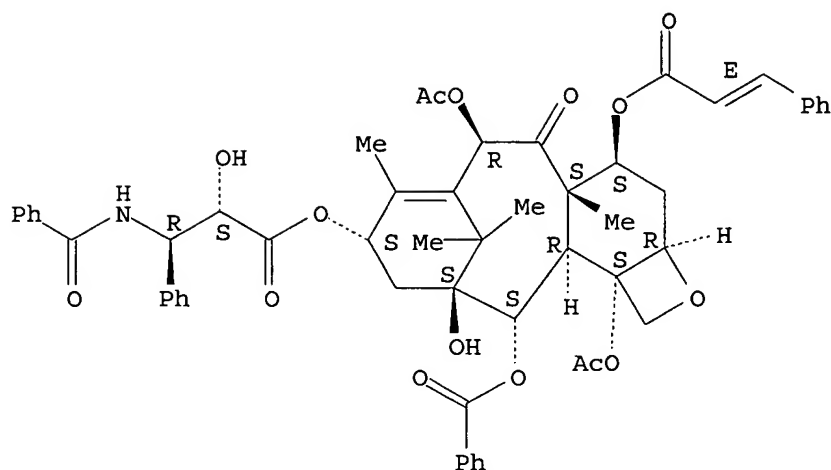
RN 618428-51-6 CAPLUS  
 CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -[[tris(1-methylethyl)silyl]oxy]-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(1-oxopentyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 618428-65-2 CAPLUS  
 CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -[[tris(1-methylethyl)silyl]oxy]-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[[ (2E)-1-oxo-3-phenyl-2-propenyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



IT 618428-04-9P 618428-05-0P 618428-51-6P  
618428-65-2P

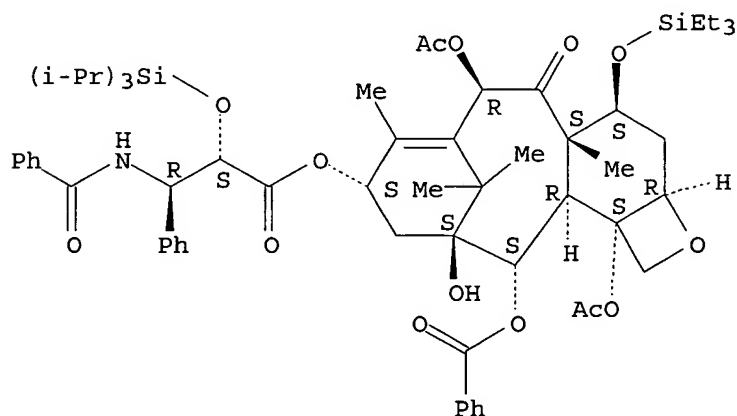
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(preparation of taxoids and their ability to activate murine macrophages and  
inhibition of the growth of macrophage-like cells)

RN 618428-04-9 CAPLUS

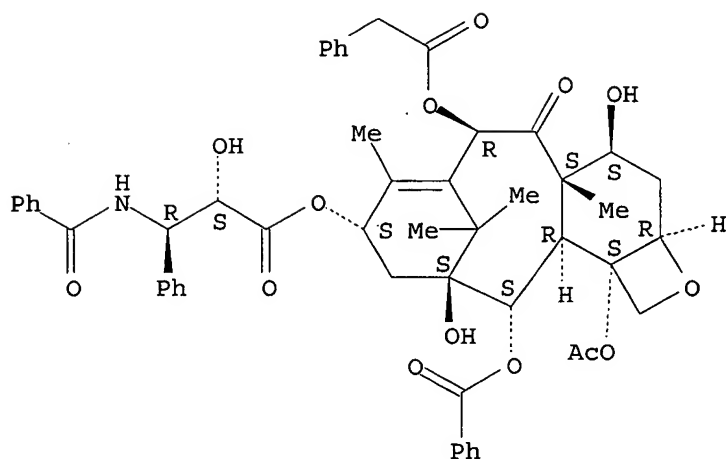
CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -[[tris(1-methylethyl)silyl]oxy]-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 618428-05-0 CAPLUS

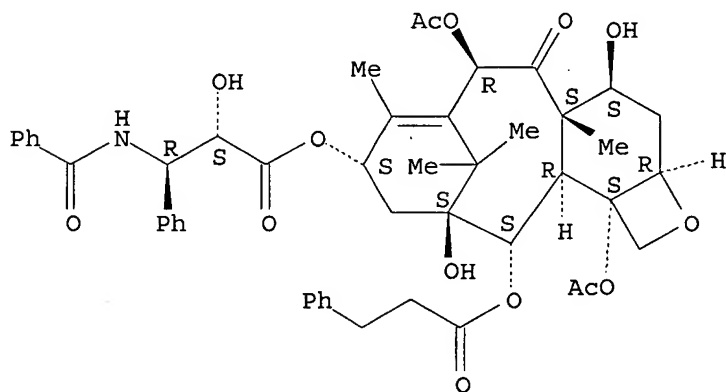
CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -[[tris(1-methylethyl)silyl]oxy]-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)



RN 618428-39-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-12-(1-oxo-3-phenylpropoxy)-7,11-methano-1H-  
cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



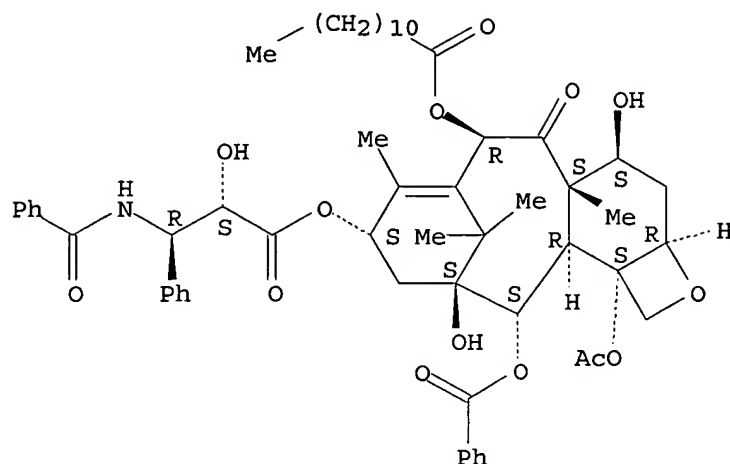
RN 618428-55-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-  
tetramethyl-5-oxo-4-[(2E)-1-oxo-3-phenyl-2-propenyl]oxy-7,11-methano-1H-  
cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

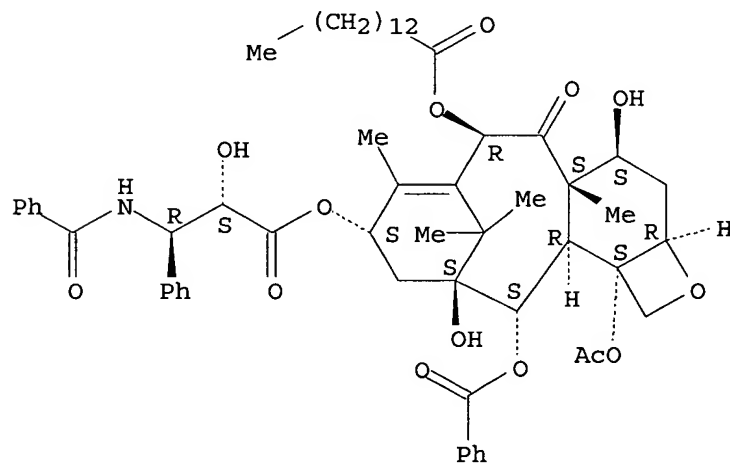
Absolute stereochemistry.



RN 618428-14-1 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-6-[(1-oxotetradecyl)oxy]-7,11-methano-1H-  
cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)-(9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

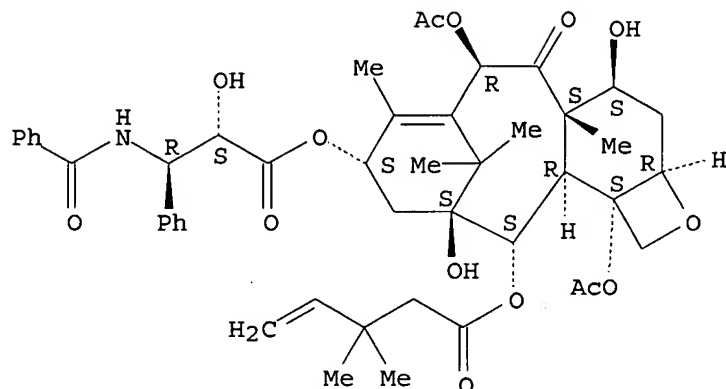


RN 618428-15-2 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-6-[(phenylacetyl)oxy]-7,11-methano-1H-  
cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)-(9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.



IT 618428-06-1P 618428-13-0P 618428-14-1P

618428-15-2P 618428-39-0P 618428-55-0P

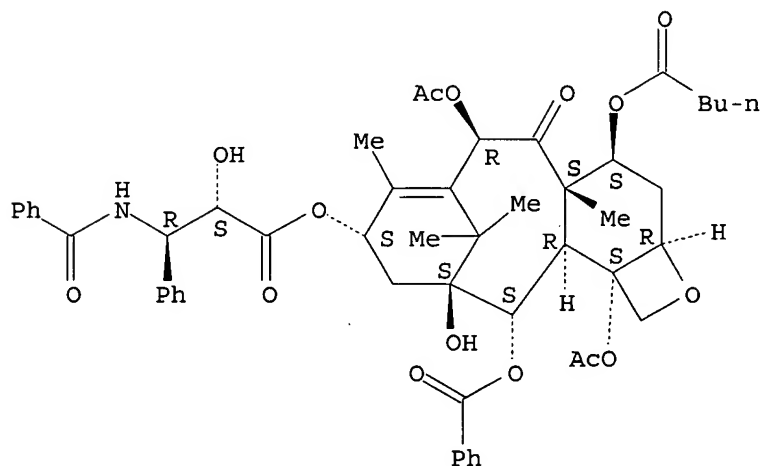
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of taxoids and their ability to activate murine macrophages and inhibition of the growth of macrophage-like cells)

RN 618428-06-1 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(1-oxopentyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 618428-13-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-6-[(1-oxododecyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)-(9CI) (CA INDEX NAME)

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:350856

AB A series of new taxoids modified at the C-3', C-3'N, C-10, C-2 and C-7 positions was designed, synthesized and evaluated for their potency to induce NO and TNF production by peritoneal murine macrophages (M $\phi$ ) from LPS-responsive C3H/HeN and LPS-hyporesponsive C3H/HeJ strains and human blood cells, and for their ability to inhibit the growth of M $\phi$ -like cell lines J774.1 and J7.DEF3. The SAR-study showed that the nature of the substituents at these positions are critical for the induction of TNF and NO production by M $\phi$ . Positions C-3' and C-10 are the most flexible, and an intriguing effect of the length of the substituents at the C-10 position is observed for taxoids bearing a straight chain alkanoyl moiety. An aromatic group at the C-3'N and C-2 positions is required for the activity, while only hydroxyl or acetyl substituents seem to be tolerated at the C-7 position. The natural stereochem. in the C-13 isoserine side chain of the taxoids is an absolute requirement for macrophage activation. There is no correlation between the ability of the taxoids to induce TNF/NO production in C3H/HeN M $\phi$  and the cytotoxicity against M $\phi$ -like cells.

IT 618428-21-0P 618428-23-2P

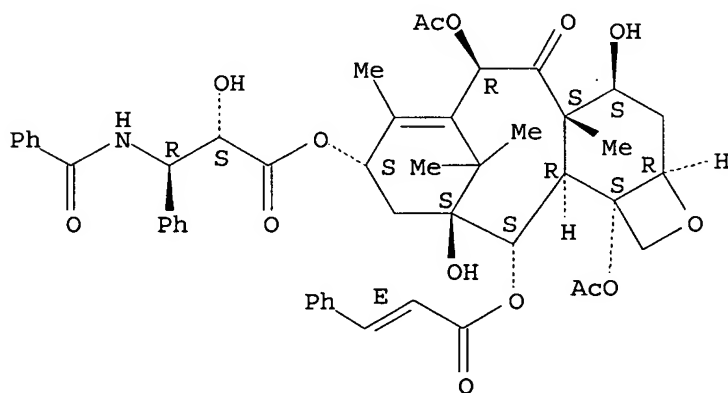
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(preparation of taxoids and their ability to activate murine macrophages and inhibition of the growth of macrophage-like cells)

RN 618428-21-0 CAPLUS

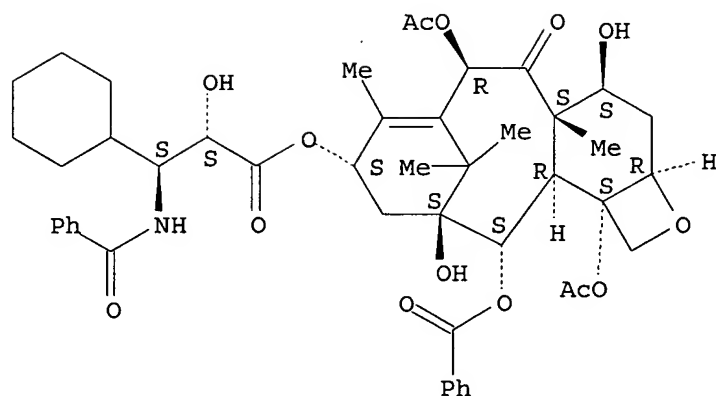
CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-12-[[[(2E)-1-oxo-3-phenyl-2-propenyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 618428-23-2 CAPLUS

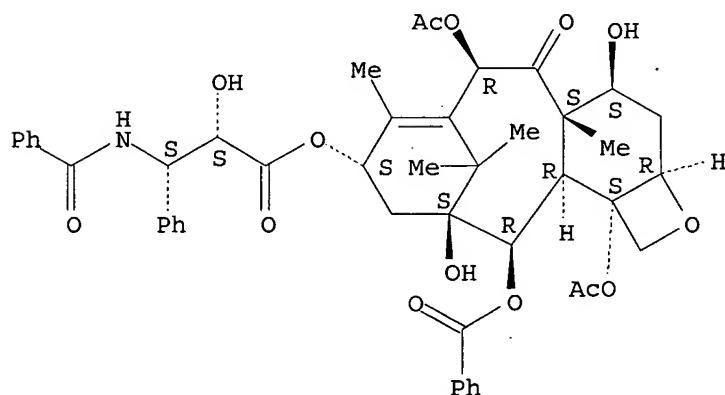
CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-[(3,3-dimethyl-1-oxo-4-pentenyl)oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)



RN 676235-24-8 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12R,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 11 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:427763 CAPLUS

DOCUMENT NUMBER: 139:350856

TITLE: Structure-activity relationship study of taxoids for their ability to activate murine macrophages as well as inhibit the growth of macrophage-like cells

AUTHOR(S): Ojima, Iwao; Fumero-Oderda, Cecilia L.; Kuduk, Scott D.; Ma, Zhuping; Kirikae, Fumiko; Kirikae, Teruo

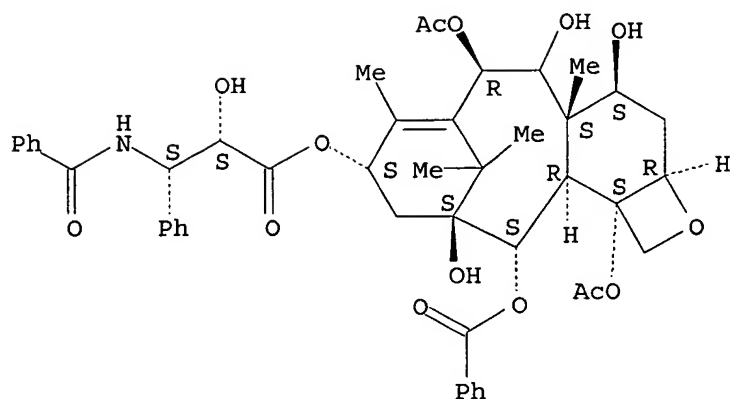
CORPORATE SOURCE: Department of Chemistry, State University of New York at Stony Brook, Stony Brook, NY, 11794-3400, USA

SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(13), 2867-2888

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

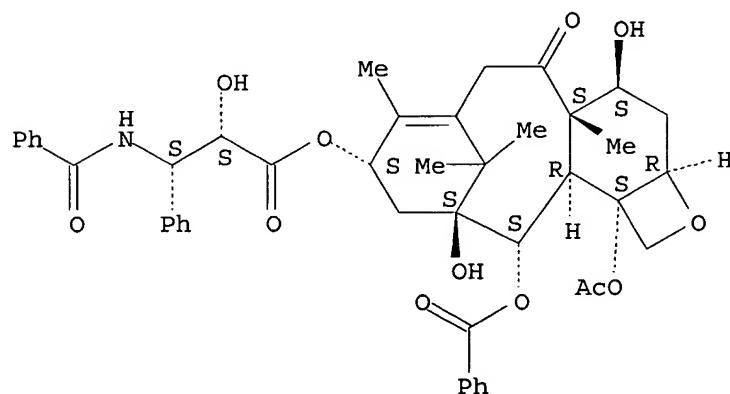
DOCUMENT TYPE: Journal



RN 675853-96-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

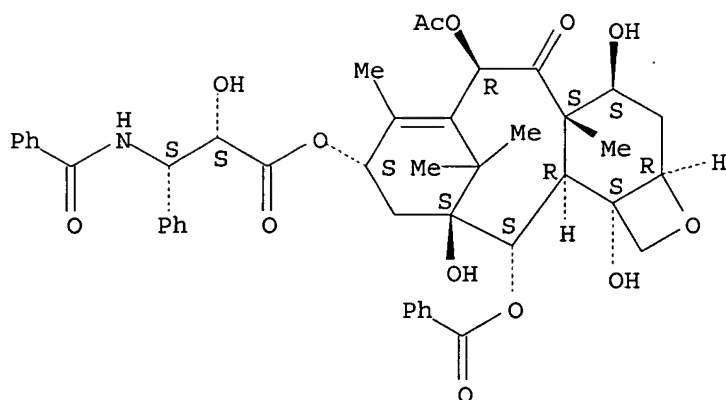


RN 675853-97-1 CAPLUS

CN Cyclohexanepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

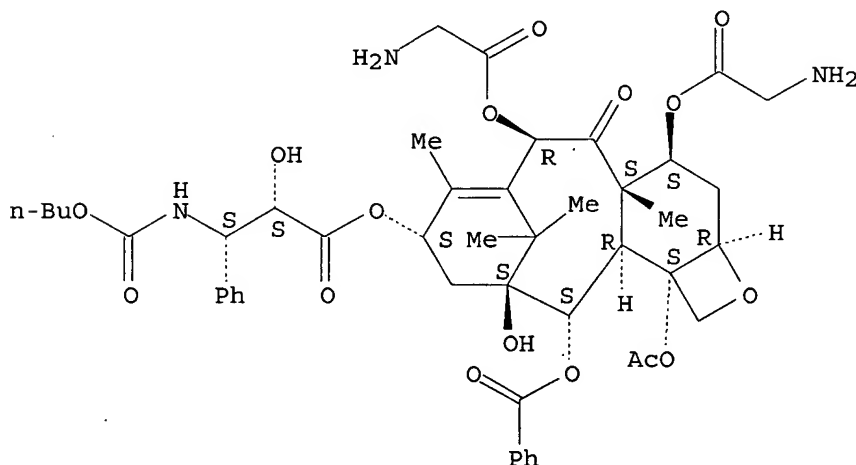




RN 675853-94-8 CAPLUS

CN Glycine, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-9-[(2S,3S)-3-[(butoxycarbonyl)amino]-2-hydroxy-1-oxo-3-phenylpropoxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxete-4,6-diyl ester (9CI) (CA INDEX NAME)

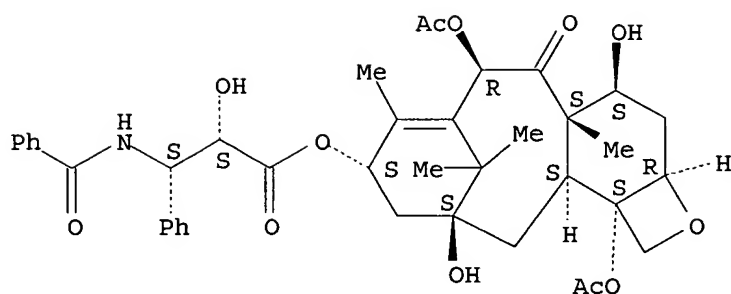
Absolute stereochemistry.



RN 675853-95-9 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,11-trihydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

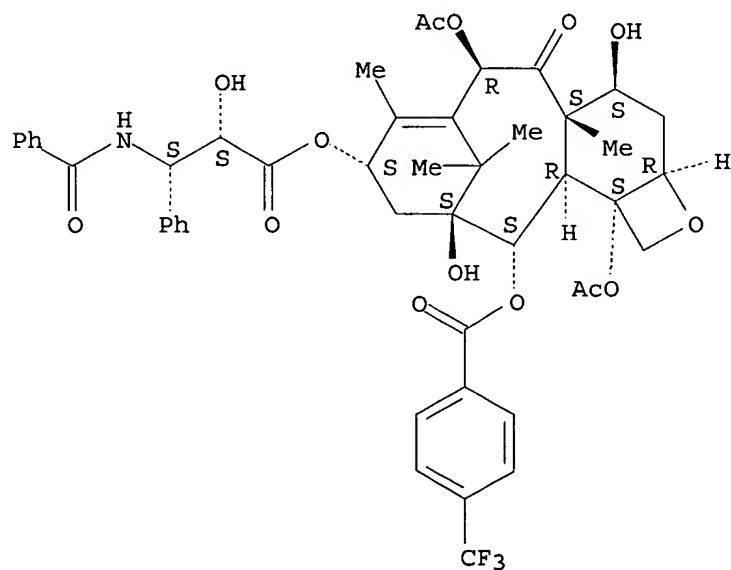
Absolute stereochemistry.



RN 675853-92-6 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-12-[[4-(trifluoromethyl)benzoyloxy]-7,11-methano-1H-  
cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.

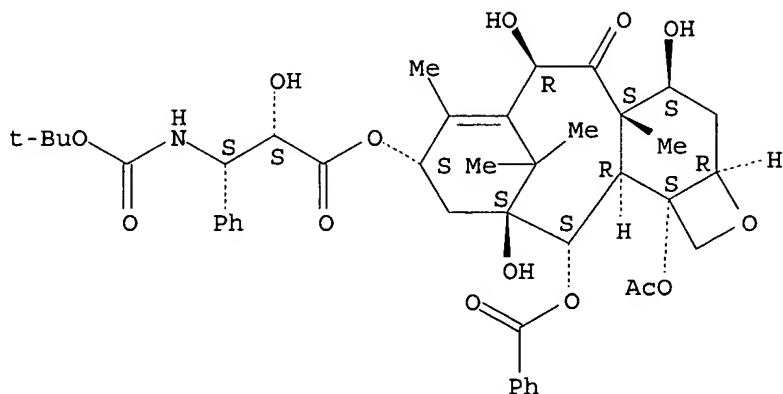


RN 675853-93-7 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6-(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11,12b-trihydroxy-  
4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-  
9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

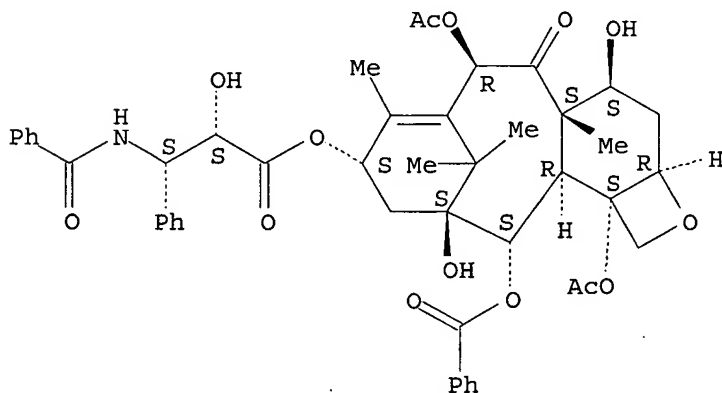
Absolute stereochemistry.



RN 179798-21-1 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

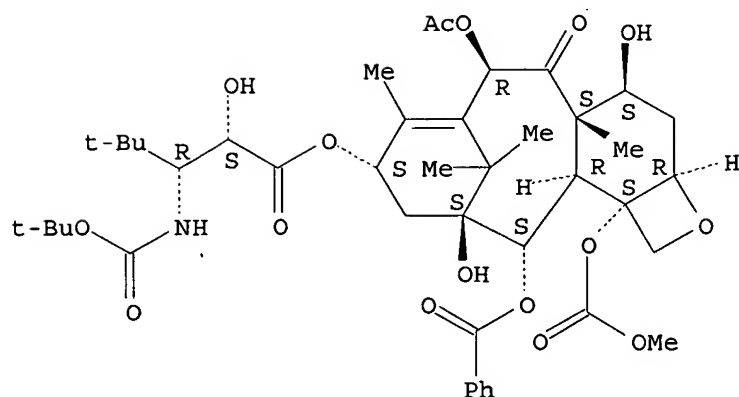
Absolute stereochemistry.



RN 675853-91-5 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12aS,12bS)-6,12b-bis(acetyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 10 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:725913 CAPLUS

DOCUMENT NUMBER: 140:280729

TITLE: 3D QSAR studies for the  $\beta$ -tubulin binding site of microtubule-stabilizing anticancer agents (MSAAs). A pseudoreceptor model for taxanes based on the experimental structure of tubulin

AUTHOR(S): Maccari, Laura; Manetti, Fabrizio; Corelli, Federico; Botta, Maurizio

CORPORATE SOURCE: Dipartimento Farmaco Chimico Tecnologico, Universita degli Studi di Siena, Siena, I-53100, Italy

SOURCE: Farmaco (2003), 58(9), 659-668

CODEN: FRMCE8; ISSN: 0014-827X

PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The antimitotic agent paclitaxel continues to play an important role in the cancer chemotherapy. However, its inefficacy on certain resistant cells and toxic side effects have led to the search of new taxanes with improved biol. activity. By a pseudoreceptor modeling approach, we have developed a binding site model for a series of taxanes. It is the first 3D QSAR model derived from the exptl. determined tubulin structure obtained by electron crystallog. studies. The model is able to correlate quant. the structural properties of the studied compds. with their biol. data.

IT 133577-33-0 179798-21-1 675853-91-5

675853-92-6 675853-93-7 675853-94-8

675853-95-9 675853-96-0 675853-97-1

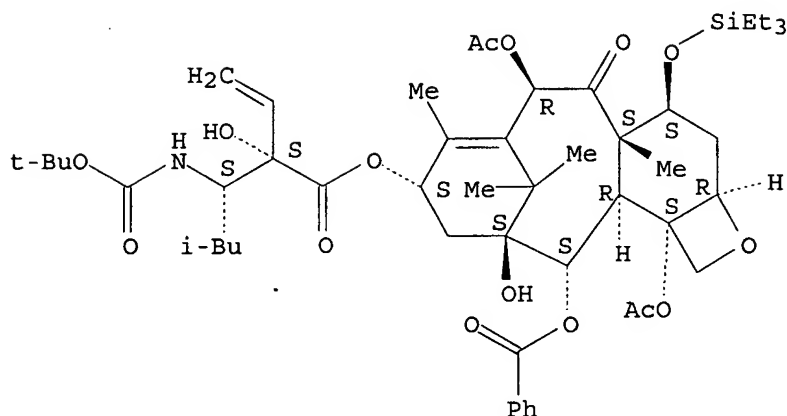
676235-24-8, 2,2'-epi-Taxol

RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)

(3D QSAR studies for the  $\beta$ -tubulin binding site of microtubule-stabilizing anticancer agents (MSAAs). a pseudoreceptor model for taxanes based on the exptl. structure of tubulin)

RN 133577-33-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 9 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:728097 CAPLUS

DOCUMENT NUMBER: 140:192359

TITLE: The discovery of BMS-275183: an orally efficacious novel taxane

AUTHOR(S): Mastalerz, Harold; Cook, Donald; Fairchild, Craig R.; Hansel, Steven; Johnson, Walter; Kadow, John F.; Long, Byron H.; Rose, William C.; Tarrant, James; Wu, Mu-Jen; Xue, May Quifen; Zhang, Guifen; Zoeckler, Mary; Vyas, Dolatrai M.

CORPORATE SOURCE: Discovery Chemistry, Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT, 06492-7660, USA

SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(20), 4315-4323

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:192359

AB The evolution of a C-4-methylcarbonate analog of paclitaxel with minimal oral bioavailability and oral efficacy, into its C-3'-t-butyl-3'-N-t-butyloxycarbonyl analog, a novel taxane with oral efficacy in preclin. models that is comparable to iv administered paclitaxel, is described.

IT 364357-78-8P

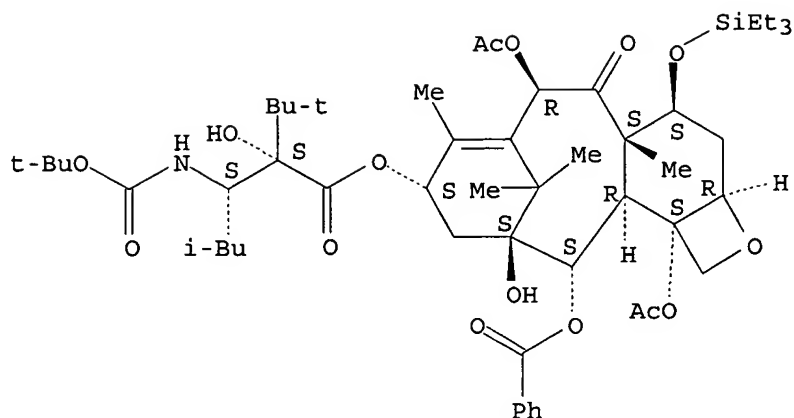
RL: SPN (Synthetic preparation); PREP (Preparation)

(discovery of BMS-275183, an orally efficacious novel taxane for cancer treatment)

RN 364357-78-8 CAPLUS

CN D-threo-Pentonic acid, 3,4,5-trideoxy-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-4,4-dimethyl-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-12b-[(methoxycarbonyl)oxy]-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester (9CI) (CA INDEX NAME)

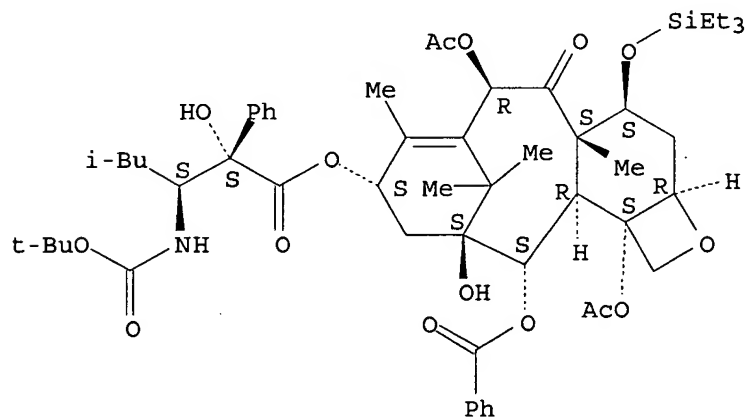
Absolute stereochemistry.



RN 849829-72-7 CAPLUS

CN Benzeneacetic acid,  $\alpha$ -[[(1S)-1-[[[(1,1-dimethylethoxy)carbonyl]amino]-3-methylbutyl]- $\alpha$ -hydroxy-], (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



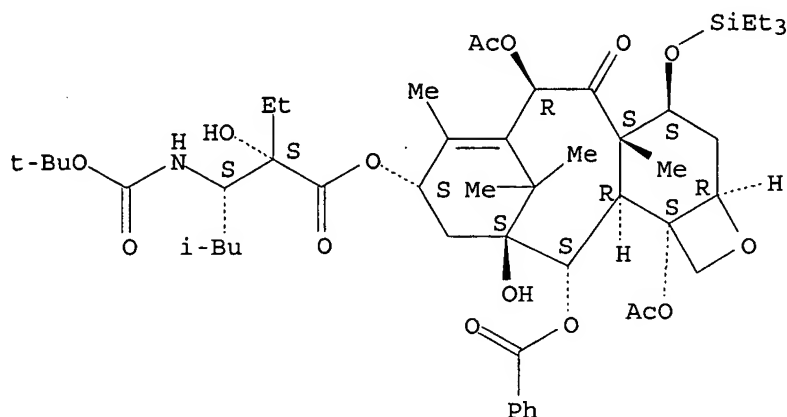
RN 849829-73-8 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-ethenyl-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2S,3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2S,3S)- (9CI) (CA INDEX NAME)

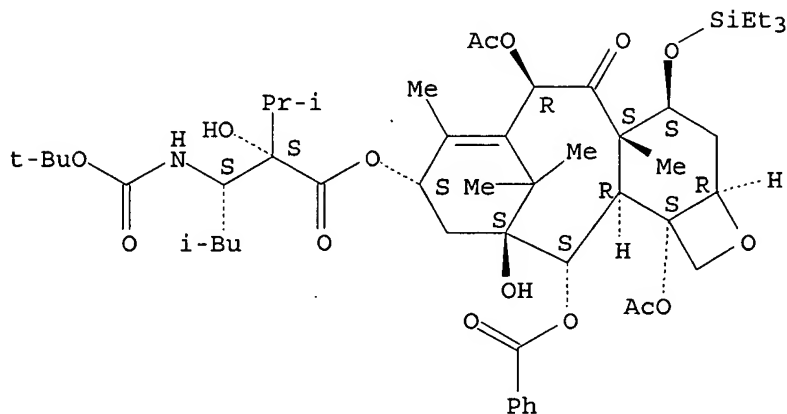
Absolute stereochemistry.



RN 849829-70-5 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy) carbonyl] amino]-2-hydroxy-5-methyl-2-(1-methylethyl)-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2S,3S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



RN 849829-71-6 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-(1,1-dimethylethyl)-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2S,3S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

2'-Substituted Taxanes as Probes for an Improved Protocol of Diastereomeric Differentiation

AUTHOR(S): Dambruoso, Paolo; Bassarello, Carla; Bifulco, Giuseppe; Appendino, Giovanni; Battaglia, Arturo; Fontana, Gabriele; Gomez-Paloma, Luigi

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Facolta di Farmacia, Universita di Salerno, Fisciano (SA), 84084, Italy

SOURCE: Organic Letters (2005), 7(6), 983-986  
CODEN: ORLEF7; ISSN: 1523-7060

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 142:392542

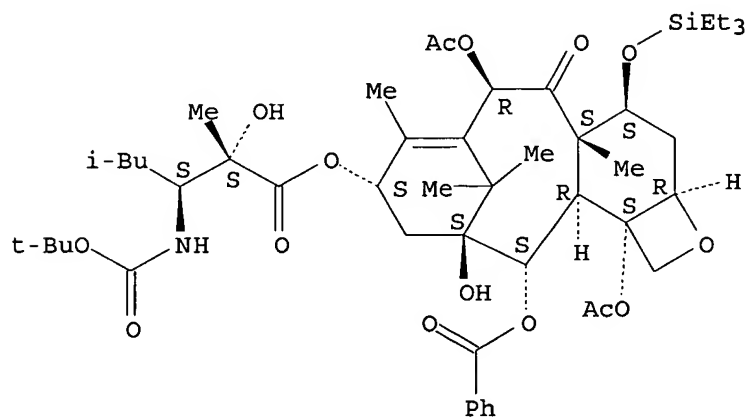
AB The configuration of the  $\alpha$ -substituted  $\alpha$ -hydroxy- $\beta$ -aminoester moiety in a series of 2'-substituted taxanes was analyzed according to the recently proposed Universal NMR Database (UDB) approach. A critical anal. of the results showed that modifications regarding chemical shift adjustment (so as to render the shifts virtually connectivity independent) were necessary to get consistent stereo-assignments in this set of compds. On this basis, a modified UDB-based strategy, especially tailored to the configurational assignment of densely substituted diastereomeric fragments, is proposed.

IT 849829-68-1P 849829-69-2P 849829-70-5P  
849829-71-6P 849829-72-7P 849829-73-8P  
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (preparation and diastereomeric differentiation of  $\alpha$ -substituted  $\alpha$ -hydroxy- $\beta$ -aminoester moiety in a series of 2'-substituted taxanes via universal NMR database approach)

RN 849829-68-1 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-2,5-dimethyl-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 849829-69-2 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-ethyl-2-hydroxy-5-methyl-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-



## (Preparation)

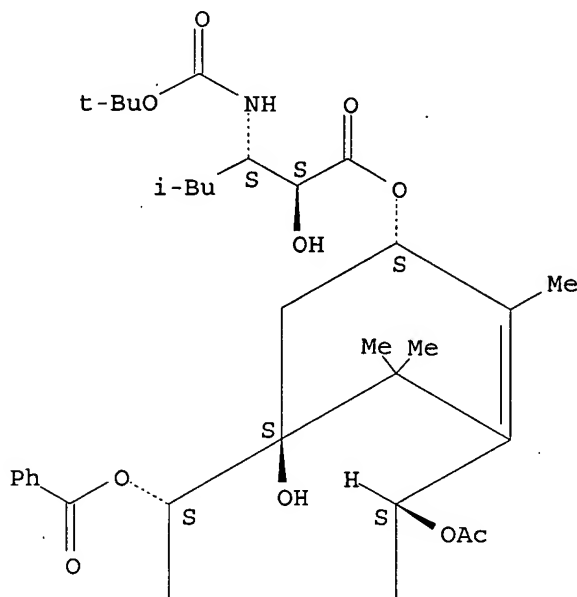
(methods for the synthesis of 9,10- $\alpha,\alpha$ -OH-taxane analogs)

RN 849213-17-8 CAPLUS

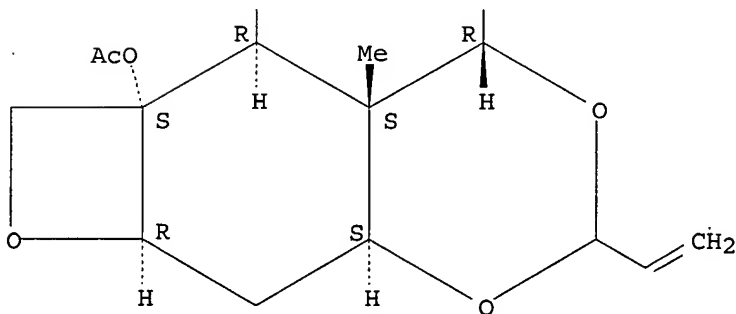
CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-, (1S,2S,4S,7S,7aR,10aS,11aR,13aS,13bR,13cS)-7,13a-bis(acetyloxy)-1-(benzyloxy)-9-ethenyl-1,3,4,7,7a,10a,11,11a,13,13a,13b,13c-dodecahydro-2-hydroxy-5,13c,14,14-tetramethyl-2,6-methano-2H-cyclodec[de]oxeto[3,2-g][1,3]benzodioxin-4-yl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

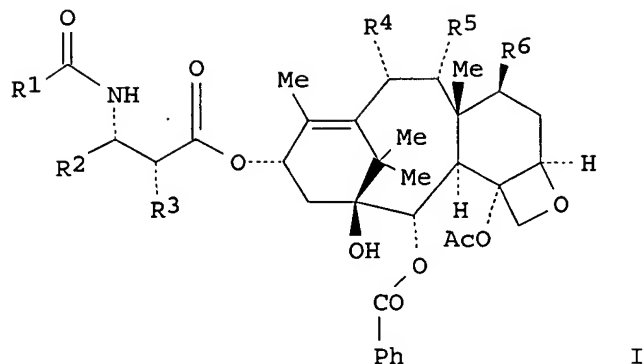


L51 ANSWER 8 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:134425 CAPLUS

DOCUMENT NUMBER: 142:392542

TITLE: Advances in the Universal NMR Database Approach.



AB The present invention relates to new taxane analogs useful for the treatment of cancer as well as methods for producing the same. The chemical compds. according to the present invention have the general formula (I) wherein R1 and R2 are each selected from H, an alkyl group, an olefinic group, an aromatic group, an O-alkyl group, an O-olefinic group, or an O-aromatic group ; R3 is hydroxyl or OP1; R4 and R5 are each hydroxyl or R7COO ; R6 is hydroxyl, OP2, R7COO, or an ether functionality ; R7 is an alkyl group, an olefinic group, or an aromatic group ; and P1 and P2 are each hydroxyl protecting groups. The chemical compds. of the present invention may particularly be 9,10- $\alpha,\alpha$ -OH taxane analogs that are formed by a process that begins with a standard taxane as the starting compound

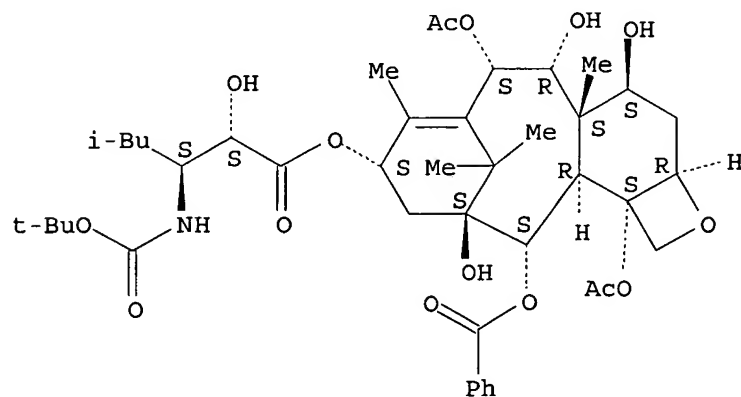
IT 849213-16-7P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(methods for the synthesis of 9,10- $\alpha,\alpha$ -OH-taxane analogs)

RN 849213-16-7 CAPLUS

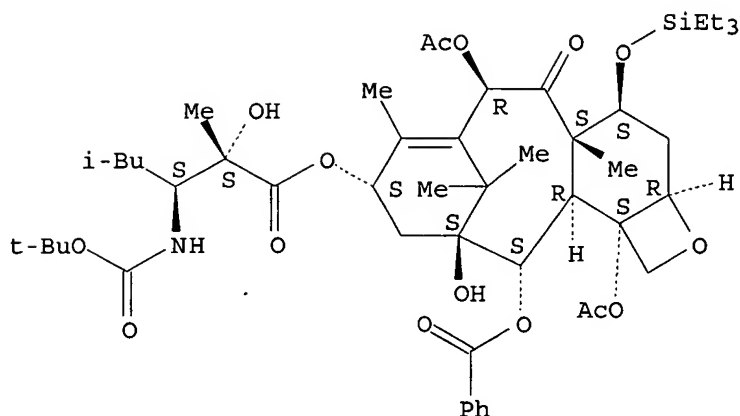
CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-5-methyl-, (2aR,4S,4aS,5R,6S,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,5,11-trihydroxy-4a,8,13,13-tetramethyl-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 849213-17-8P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 7 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:300206 CAPLUS

DOCUMENT NUMBER: 142:373994

TITLE: Methods for the synthesis of 9,10- $\alpha,\alpha$ -OH-taxane analogs

INVENTOR(S): McChesney, James D.; Ferrara, James; Zygmunt, Jan

PATENT ASSIGNEE(S): Tapestry Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030150	A2	20050407	WO 2004-US31816	20040927
WO 2005030150	A3	20050714		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004275881	A1	20050407	AU 2004-275881	20040927
CA 2539975	AA	20050407	CA 2004-2539975	20040927
US 2005148657	A1	20050707	US 2004-951555	20040927
EP 1664033	A2	20060607	EP 2004-789167	20040927
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
PRIORITY APPLN. INFO.:			US 2003-506680P	P 20030925
			WO 2004-US31816	W 20040927

OTHER SOURCE(S): MARPAT 142:373994

GI

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 6 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:336451 CAPLUS

DOCUMENT NUMBER: 143:26745

TITLE: 2'-Methyl taxanes: synthesis and NMR configurational assignment

AUTHOR(S): Dambruoso, Paolo; Bassarello, Carla; Bifulco, Giuseppe; Appendino, Giovanni; Battaglia, Arturo; Guerrini, Andrea; Fontana, Gabriele; Gomez-Paloma, Luigi

CORPORATE SOURCE: DISCAFF, Facolta di Farmacia, Universita del Piemonte Orientale, Largo Donegani, Novara, 2-28100, Italy

SOURCE: Tetrahedron Letters (2005), 46(19), 3411-3415

CODEN: TELEAY; ISSN: 0040-4039

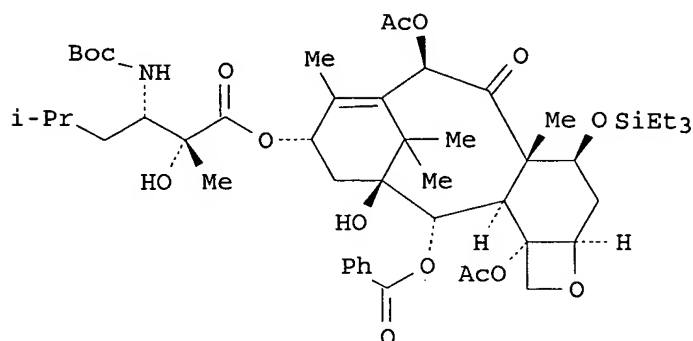
PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:26745

GI



I

AB Capitalizing on an oxidation-alkylation approach, a non-diastereoselective entry into 2'-Me taxanes, e.g. I, was developed. The issue of configurational assignment at the newly formed side-chain quaternary stereocenter was solved and put into a more general context by integrating information from an alternative diastereoselective synthesis of model compds. and from spectroscopic measurements, critically comparing the J-Based and the Universal NMR Database approaches.

IT 849829-68-1P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis and NMR configurational assignments of 2'-Me taxanes)

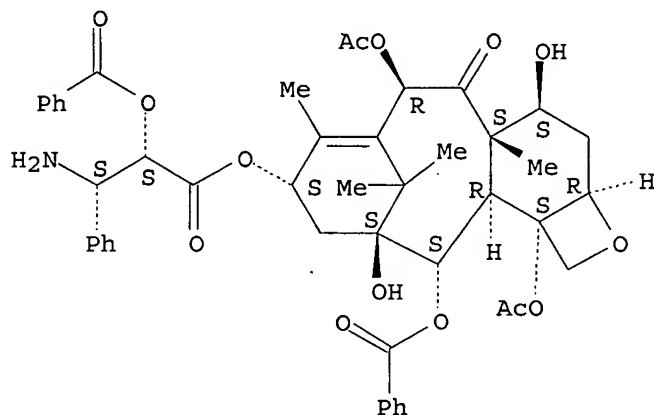
RN 849829-68-1 CAPLUS

CN Hexanoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-2,5-dimethyl-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 179551-57-6 CAPLUS  
 CN Benzenepropanoic acid,  $\beta$ -amino- $\alpha$ -(benzoyloxy)-,  
 (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
 ester, hydrochloride, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

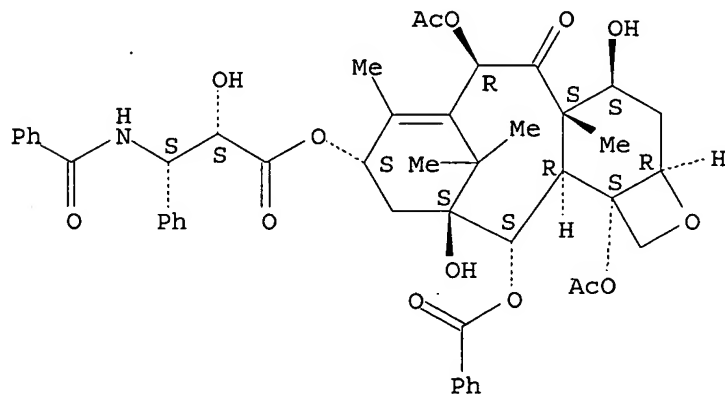


● HCl

IT 179798-21-1P, 2'-epi-Paclitaxel  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation or C(2')-hydroxyl group inversion of; method for inverting the  
 C(2')-hydroxyl group of taxane esters)

RN 179798-21-1 CAPLUS  
 CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
 (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
 ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



DOCUMENT NUMBER: 142:411508  
 TITLE: Method for inverting the C(2')-hydroxyl group of taxane esters  
 INVENTOR(S): Mcchesney, James D.; Chander, Madhavi C.; Henri, John T.; Ferrara, James V.; Brinkman, Herbert R.  
 PATENT ASSIGNEE(S): Mayne Pharma USA, Inc., USA  
 SOURCE: PCT Int. Appl., 27 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037840	A1	20050428	WO 2004-US33858	20041014
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2003-511888P P 20031016

OTHER SOURCE(S): CASREACT 142:411508; MARPAT 142:411508

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The present invention provides a method for inverting the 2'-hydroxy position of selected taxanes via cyclization of the side chain into an oxazole. The method comprises: protecting the 2' hydroxyl group of a first selected taxane I [P = H, R1 = alkyl, olefin, aromatic, O-alkyl, O-olefin, O-aromatic; R2 = H, alkyl, olefin, aromatic; R3 = taxane backbone (e.g., Baccatin III)] with a hydroxyl protecting group, such as a sulfonate. The protected taxane compound I [P = tosyl, mesyl, nosyl] is then converted to an oxazole compound II having an oxazole ring. The oxazole ring is then opened by an appropriate process, such as by hydrolyzing the oxazole compound thereby to form an intermediate compound e.g. amine salt III·HA [A = anion of an acid], which is then converted to a second taxane IV. Alternatively, the method may be used to convert the second taxane into the first taxane via intermediates V and VI·HA. The intermediate compound may be an amine salt (III·HA or VI·HA) that is treated with a base to form the second taxane. The method contemplated by be used to convert 2'-epi-paclitaxel into paclitaxel. Alternatively, the method may be used to convert paclitaxel into 2'-epi-paclitaxel. The present invention also relates to novel compds. and intermediates formed by the process.

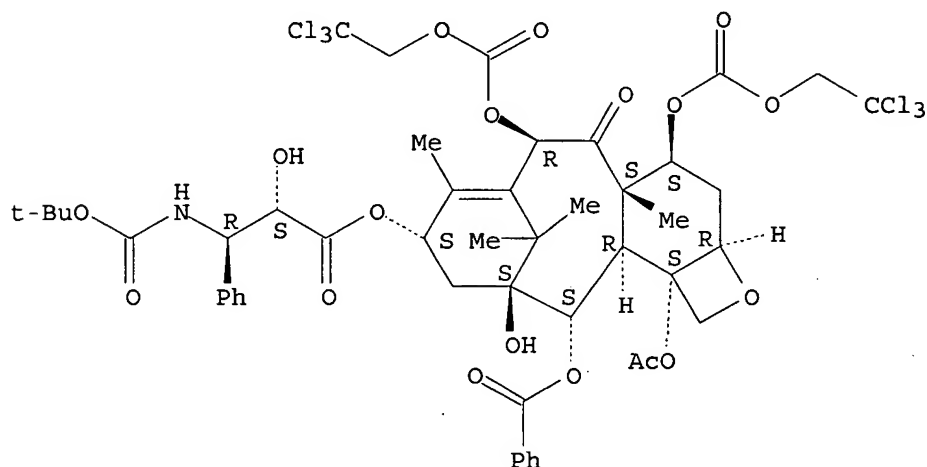
IT 179551-57-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and benzoyl group migration in; method for inverting the C(2')-hydroxyl group of taxane esters)

(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4,6-bis[[[(2,2,2-trichloroethoxy) carbonyl]oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 114977-29-6P

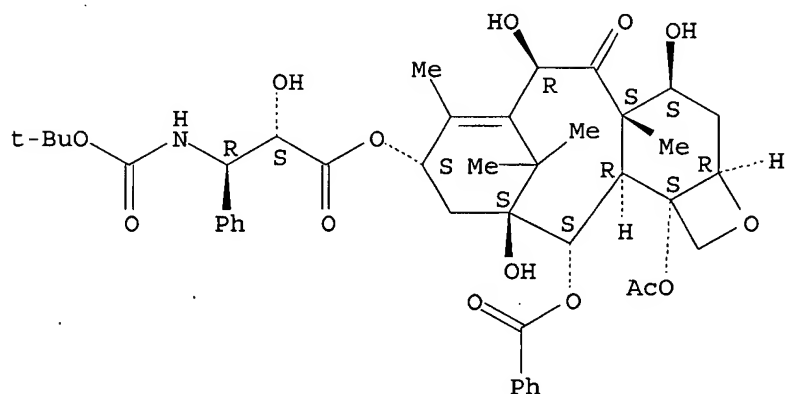
RL: SPN (Synthetic preparation); PREP (Preparation)

(novel method to synthesize docetaxel and its isomer with high yields)

RN 114977-29-6 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy) carbonyl] amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



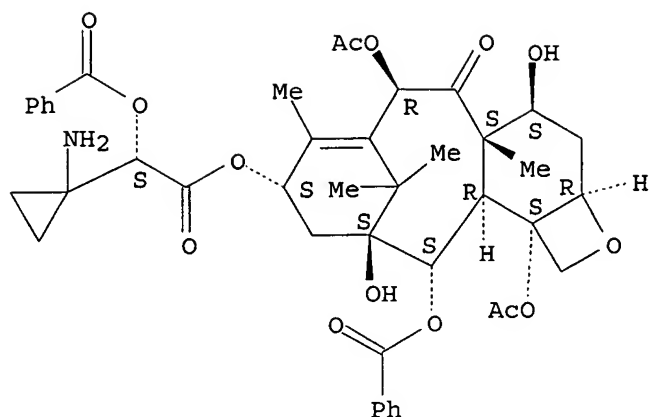
REFERENCE COUNT:

10

THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 5 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:371264 CAPLUS



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 4 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:489165 CAPLUS

DOCUMENT NUMBER: 143:153531

TITLE: A novel method to synthesize docetaxel and its isomer with high yields

AUTHOR(S): Qi, Chuan-Min; Wang, Yun-Feng; Yang, Ling-Chun

CORPORATE SOURCE: Department of Chemistry, Beijing Normal University, Beijing, 100875, Peop. Rep. China

SOURCE: Journal of Heterocyclic Chemistry (2005), 42(4), 679-684

CODEN: JHTCAD; ISSN: 0022-152X

PUBLISHER: HeteroCorporation

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:153531

AB Side chains of docetaxel and its isomer were obtained through Staudinger cycloaddn. and catalytic hydrogenation of chlorophenyl intermediates, using chlorobenzaldehyde as starting material. Syntheses of three novel chiral azetidinone derivs. through the Staudinger cycloaddn. reaction of chlorophenyl chiral amine Schiff base with different substituted positions were described and their ring-opening reaction under the catalysis of Pd/MgCO<sub>3</sub> or Pd/C to afford side chains of docetaxel and its isomer in high yields was investigated. Finally, docetaxel and its isomer were obtained. Single crystal of (3S,4R)-3-hydroxy-N-[(S)-(1-phenyl)ethyl]-4-(2'-chlorophenyl)-2-azetidinone was obtained, the configuration of which was determined by X-ray diffraction. Because of the mild cyclization reaction condition and convenient asym. resolution operation when p-chlorobenzaldehyde was employed instead of benzaldehyde, the yield of cyclization and hydrogenation increased dramatically and the total yield of docetaxel was higher than the result in literature. When o-chlorobenzaldehyde was employed instead of benzaldehyde an isomer of docetaxel was obtained by the same way.

IT 114977-25-2P

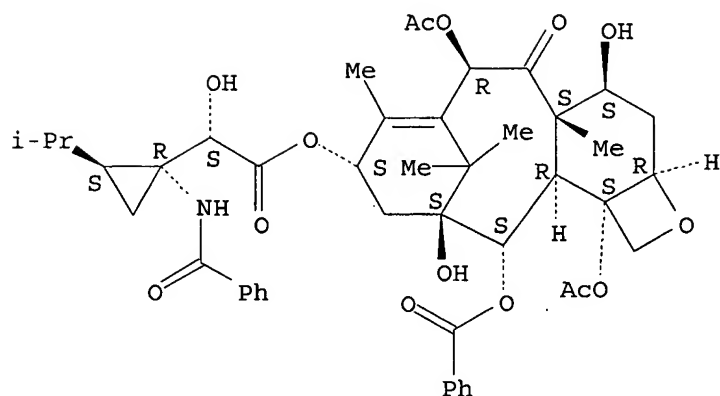
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(novel method to synthesize docetaxel and its isomer with high yields)

RN 114977-25-2 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-

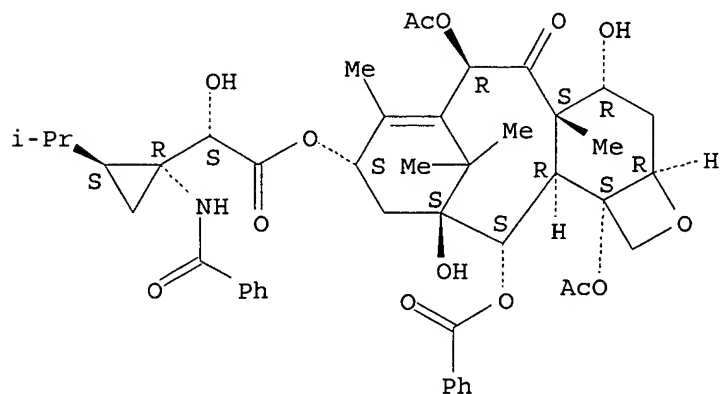




RN 869735-09-1 CAPLUS

CN Cyclopropaneacetic acid, 1-(benzoylamino)- $\alpha$ -hydroxy-2-(1-methylethyl)-, (2aR,4R,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S,1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 534572-19-5P

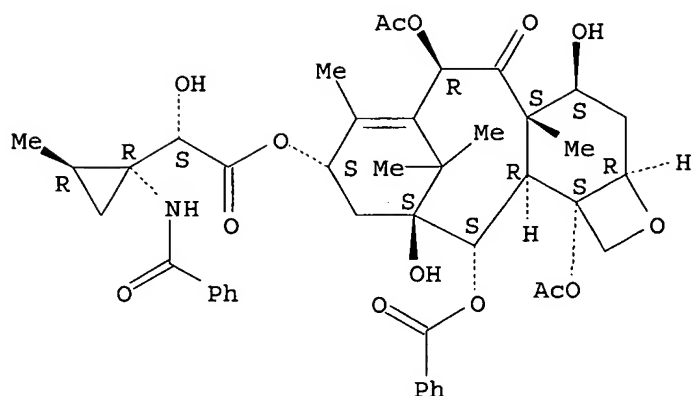
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and anticancer activity of C3'-cyclopropanated taxol analogs)

RN 534572-19-5 CAPLUS

CN Cyclopropaneacetic acid, 1-amino- $\alpha$ -(benzoyloxy)-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

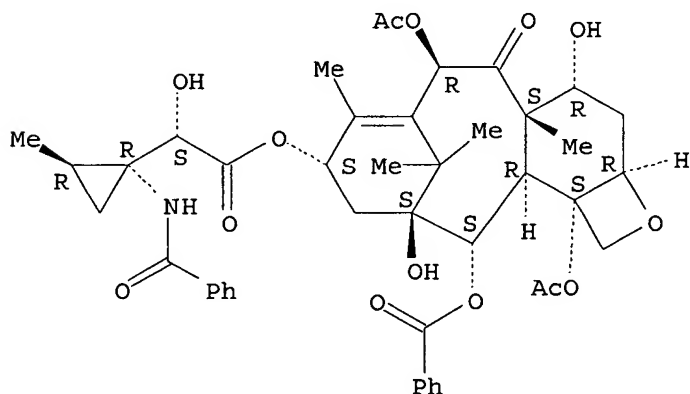
Absolute stereochemistry.



RN 869735-07-9 CAPLUS

CN Cyclopropaneacetic acid, 1-(benzoylamino)- $\alpha$ -hydroxy-2-methyl-, (2aR,4R,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S,1R,2R)-(9CI) (CA INDEX NAME)

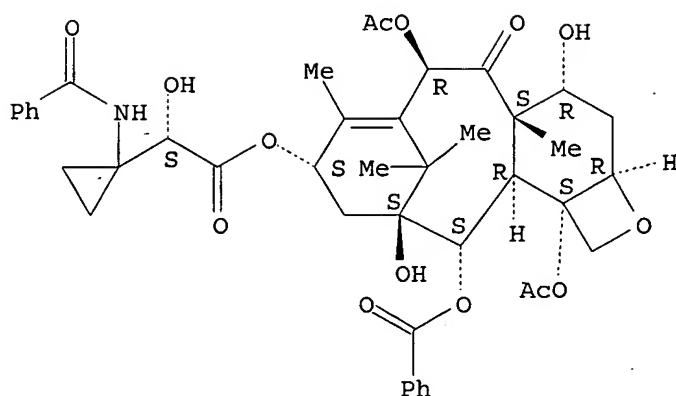
Absolute stereochemistry. Rotation (-).



RN 869735-08-0 CAPLUS

CN Cyclopropaneacetic acid, 1-(benzoylamino)- $\alpha$ -hydroxy-2-(1-methylethyl)-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S,1R,2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



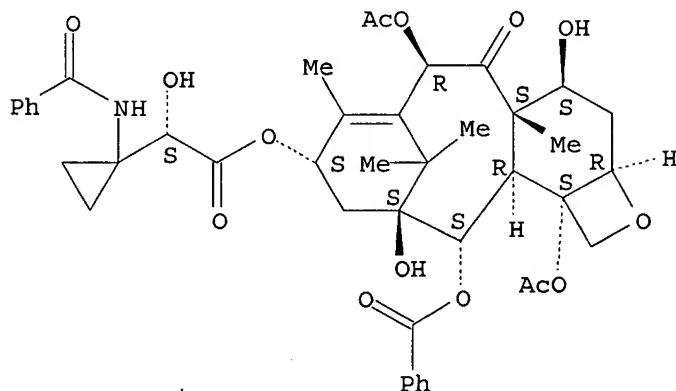
IT 534572-23-1P 869735-06-8P 869735-07-9P  
869735-08-0P 869735-09-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL  
(Biological study); PREP (Preparation)  
(preparation and anticancer activity of C3'-cyclopropanated taxol analogs)

RN 534572-23-1 CAPLUS

CN Cyclopropaneacetic acid, 1-(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

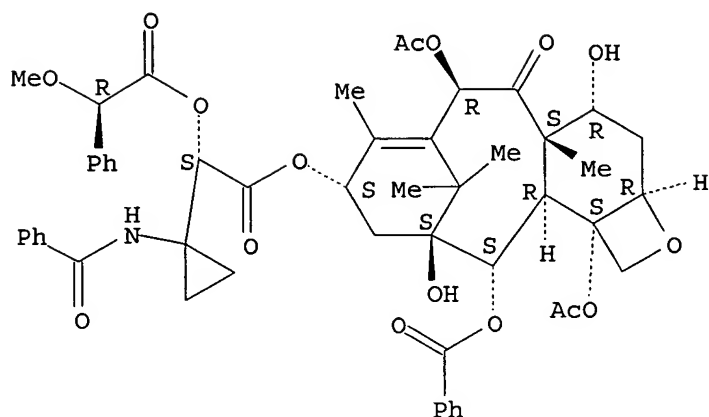
Absolute stereochemistry. Rotation (-).



RN 869735-06-8 CAPLUS

CN Cyclopropaneacetic acid, 1-(benzoylamino)- $\alpha$ -hydroxy-2-methyl-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, ( $\alpha$ S,1R,2R)- (9CI) (CA INDEX NAME)

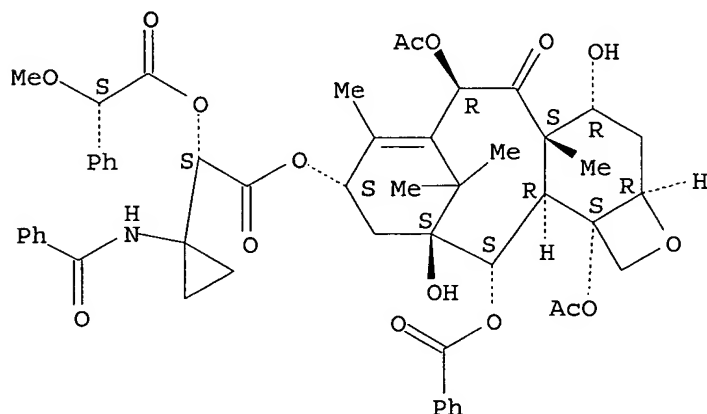
Absolute stereochemistry. Rotation (-).



RN 534572-30-0 CAPLUS

CN Benzeneacetic acid,  $\alpha$ -methoxy-, (1S)-1-[1-(benzoylamino)cyclopropyl]-2-[[[(2aR,4R,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl]oxy]-2-oxoethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 534572-25-3P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and anticancer activity of C3'-cyclopropanated taxol analogs)

RN 534572-25-3 CAPLUS

CN Cyclopropaneacetic acid, 1-(benzoylamino)- $\alpha$ -hydroxy-, (2aR,4R,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Lakdawala, Ami; Snyder, James P.; Bane, Susan L.;  
Shanker, Natasha; Ravindra, Rudravajhala; Kingston,  
David G. I.

CORPORATE SOURCE:

Department of Chemistry, M/C 0212, Virginia  
Polytechnic Institute and State University,  
Blacksburg, VA, 24061, USA

SOURCE:

European Journal of Organic Chemistry (2005), (18),  
3962-3972

CODEN: EJOCFK; ISSN: 1434-193X

PUBLISHER:

Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE:

Journal

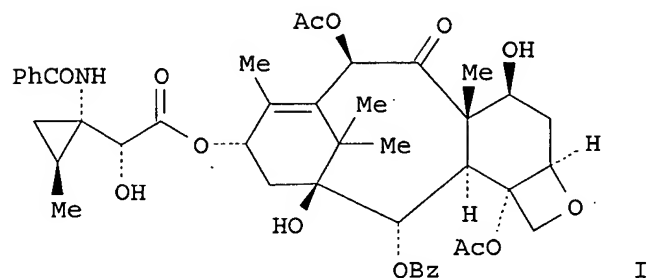
LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 144:6936

GI



I

AB Ten taxoids with a cyclopropanated side chain were synthesized by coupling a spirocyclopropanated oxazoline-5-carboxylic acid with 7-(triethylsilyl)baccatin III, followed by hydrolytic ring opening and benzoyl migration. The absolute configuration of the 2'-position was determined by

NMR anal. of the corresponding Mosher esters. These paclitaxel analogs were active in A2780 mammalian and PC-3 prostate cancer cell lines, and also in a tubulin-assembly assay, but all the analogs were less active than paclitaxel itself. To probe the basis for the uniform potency reduction shown by the cyclopropanated taxoid series, we have examined the conformational properties of compound I alone by mol. mechanics and in complex with tubulin by mol. dynamics. In addition, we have performed an NMR/NAMFIS conformer deconvolution anal. for compound I. Both modeling and NAMFIS approaches provide a satisfying understanding of the biol. behavior of the series of cyclopropanated taxoids and provide further, though indirect, support for the T-form as characteristic of taxoids bound to  $\beta$ -tubulin.

IT 534572-29-7P 534572-30-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and absolute configuration of)

RN 534572-29-7 CAPLUS

CN Benzeneacetic acid,  $\alpha$ -methoxy-, (1S)-1-[1-(benzoylamino)cyclopropyl]-2-[[[(2aR,4R,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl]oxy]-2-oxoethyl ester, ( $\alpha$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

AUTHOR(S): Xu, Xuan; Xu, Zhi-guang; Luo, Yi-fan  
 CORPORATE SOURCE: School of Chemistry and Environment, South China Normal University, Guangzhou, 510631, Peop. Rep. China  
 SOURCE: Huanan Shifan Daxue Xuebao, Ziran Kexueban (2005), (4), 73-80  
 CODEN: HSDZER; ISSN: 1000-5463  
 PUBLISHER: Huanan Shifan Daxue  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Chinese

AB After the MM3 geometry optimizing, the electronic structures of 43 taxol analogs have been calculated by MNDO quantum chemical method. The BP artificial

neural network pattern recognition has been performed for analyzing the QSAR of taxol analog anti-tumor drugs. It can be concluded as follows: (1) The relationship between logPT values of C13 side chain in taxol analogs and activity follows the parabola model ( $Popt = 3.14$ ). The more neg. charge of Bz on 2 - OBz and pos. charge of C1 and C3' atoms of taxol analogs, the higher activities they will have. R1, R2, 1 - OH and 2 - OBz may be the important active sites of the mols. The BP artificial neural network pattern recognition has a 98% accuracy, which may predict the activities of taxol analogs.

IT 133577-33-0

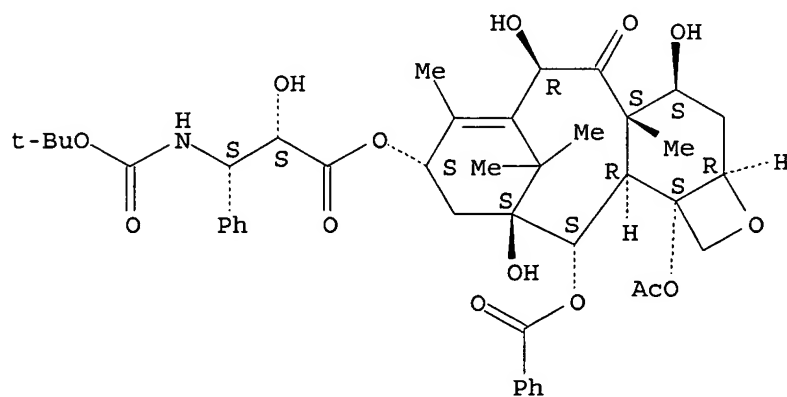
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neural network pattern recognition study on quant. structure - activity relationships of taxol analog anti-tumor drugs)

RN 133577-33-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L51 ANSWER 3 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1082693 CAPLUS

DOCUMENT NUMBER: 144:6936

TITLE: C-3'-cyclopropanated taxol analogs: Synthesis, bioassay and biostructural analysis

AUTHOR(S): Liu, Changhui; Tamm, Markus; Notzel, Marcus W.; Rauch, Karsten; de Meijere, Armin; Schilling, Jennifer K.;

CORPORATE SOURCE: Department of Analytical Research, Discovery Research,  
Dr. Reddy's Laboratories Ltd., Hyderabad, Andhra  
Pradesh, 500049, India  
SOURCE: Journal of Pharmaceutical and Biomedical Analysis  
(2006), 40(3), 614-622  
CODEN: JPBADA; ISSN: 0731-7085  
PUBLISHER: Elsevier B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB During the process development of docetaxel, two polar impurities (Impurities I and II) and two non-polar impurities (Impurities III and IV) were detected by high performance liquid chromatog. (HPLC). All the impurities were isolated by Medium Pressure Liquid Chromatog. (MPLC). The Impurities I, II, III and IV were identified as 13-[(4S,5R)-2-oxo-4-phenyl-oxazolidine-5-carboxyl]-10-deacetyl baccatin III ester, 2'-epi docetaxel, 7-epi docetaxel and 13-[(4S,5R)-2-oxo-4-phenyl-oxazolidine-3,5-dicarboxyl-3-tert-butyl]-10-deacetyl baccatin III ester, resp., based on one- (1D) and two-dimensional (2D) NMR spectroscopy data. The Impurity IV was crystallized and the structure was solved by single crystal X-ray diffraction (XRD). Two impurities (Impurities II and III) were found to be process related, while the remaining two impurities (Impurities I and IV) turned out to be isomers. The formation of these impurities was discussed.

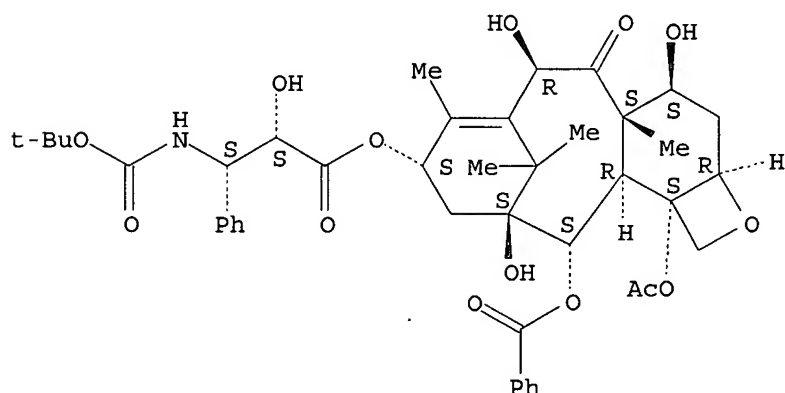
IT 133577-33-0

RL: ANT (Analyte); ANST (Analytical study)  
(determination of impurities in docetaxel by HPLC)

RN 133577-33-0 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, ( $\alpha$ S, $\beta$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 2 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

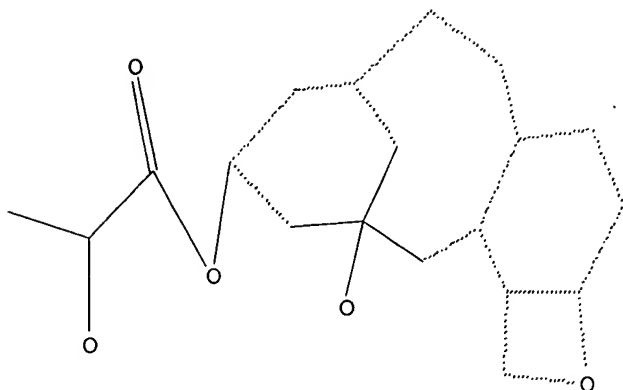
ACCESSION NUMBER: 2006:46697 CAPLUS

DOCUMENT NUMBER: 144:460276

TITLE: Neural network pattern recognition study on the quantitative structure - activity relationships of taxol analogue anti-tumor drugs

=> d stat que L24

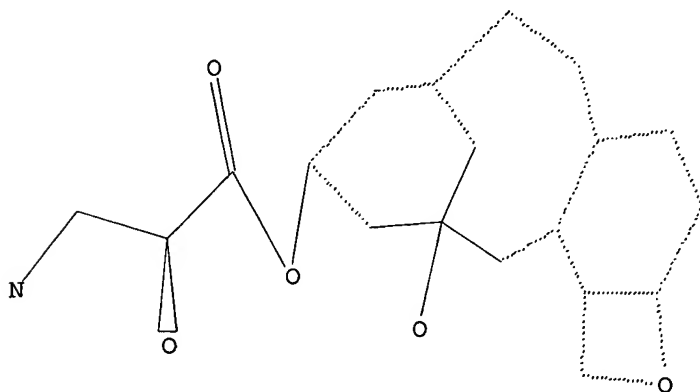
L3 STR



Structure attributes must be viewed using STN Express query preparation.

L5 7665 SEA FILE=REGISTRY SSS FUL L3

L20 STR



Structure attributes must be viewed using STN Express query preparation.

L22 111 SEA FILE=REGISTRY SUB=L5 SSS FUL L20

L24 59 SEA FILE=CAPLUS ABB=ON PLU=ON L22

=> s L24 not L49

L51 52 L24 NOT L49

=> d ibib abs hitstr L51 1-52

L51 ANSWER 1 OF 52 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:160274 CAPLUS

DOCUMENT NUMBER: 144:419879

TITLE: Isolation and characterization of impurities in docetaxel

AUTHOR(S): Vasu Dev, R.; Moses Babu, J.; Vyas, K.; Sai Ram, P.; Ramachandra, P.; Sekhar, N. M.; Mohan Reddy, D. N.; Srinivasa Rao, N.



# STRUCTURE SEARCH #1

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<http://www.cas.org/ONLINE/UG/regprops.html>

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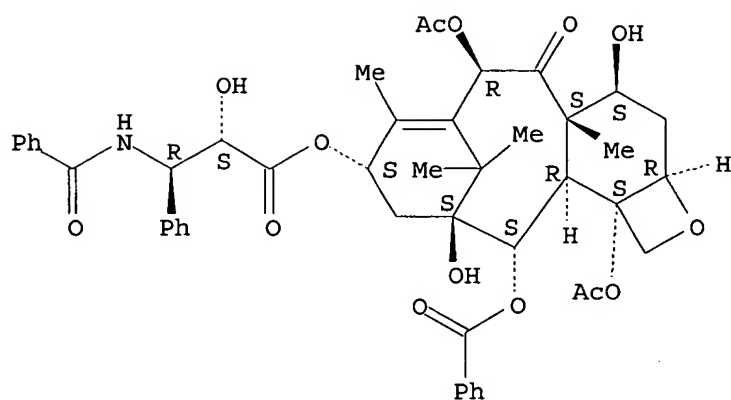
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FILE LAST UPDATED: 18 Sep 2006 (20060918/ED)

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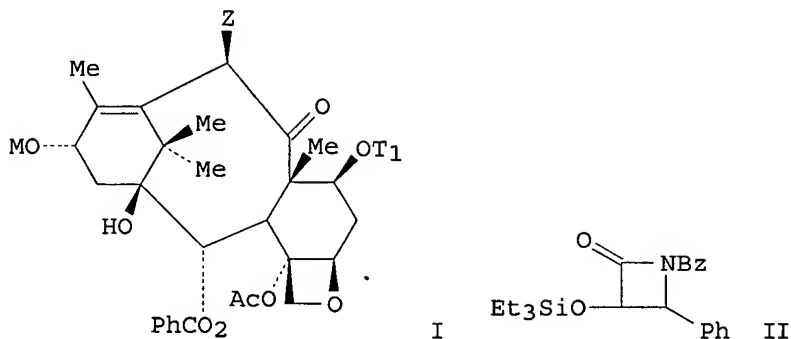
<http://www.cas.org/infopolicy.html>  
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE



IC ICM C07D305-14  
 CC 30-20 (Terpenes and Terpenoids)  
 Section cross-reference(s): 63  
 IT 114977-28-5P, Taxotere **149197-23-9P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

CS 1994-661	A 19920922
EP 1992-921316	A3 19920922
EP 1998-114788	A3 19920922
JP 1993-506299	A3 19920922
US 1992-949107	B3 19920922
WO 1992-US7952	A 19920922
US 1992-967998	B1 19921026
WO 1994-US2382	W 19940304
US 1994-263270	B1 19940621
US 1994-314532	A1 19940928
US 1994-351532	A3 19941207
US 1995-483309	A3 19950607
US 1996-607108	A1 19960226
US 1997-941640	A1 19970930
US 2000-517791	A1 20000302
US 2000-566970	A1 20000509
US 2002-194343	A1 20020712
US 2002-289103	A1 20021106

OTHER SOURCE(S): MARPAT 119:117582.  
GI



AB A metal alkoxide I (T1 = H, hydroxy protecting group; Z = OT2, O2CMe; T2 = H, hydroxy protecting group; M = Group IA, IIA, transition metal) are useful in the preparation of biol. active derivs. of baccatin III and 10-deacetylbaccatin III. Thus, treating 7-(triethylsilyl)baccatin III with K hexamethyldisilazide followed by azetidinone II gave 90% (2'R,3'S)-2',7-bis(triethylsilyl)taxol.

IT 149197-23-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 149197-23-9 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

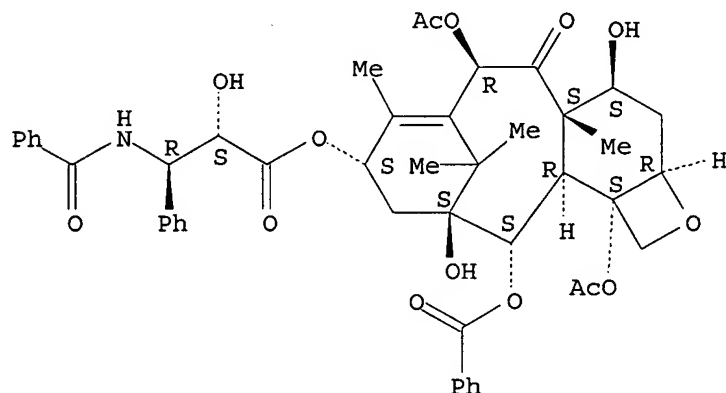
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CA 2098568	C	19970603		
AU 9226888	A1	19930427	AU 1992-26888	19920922
AU 643911	B2	19931125		
US 5274124	A	19931228	US 1992-949066	19920922
EP 605638	A1	19940713	EP 1992-921317	19920922
EP 605638	B1	19990901		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
HU 66398	A2	19941128	HU 1994-831	19920922
JP 07502982	T2	19950330	JP 1993-506277	19920922
JP 3320416	B2	20020903		
EP 884314	A2	19981216	EP 1998-114788	19920922
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EP 884314	B1	20040121		
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AT 184004	E	19990915	AT 1992-921317	19920922
ES 2137951	T3	20000101	ES 1992-921317	19920922
CZ 287417	B6	20001115	CZ 1994-660	19920922
CZ 287609	B6	20010117	CZ 1994-661	19920922
CZ 289299	B6	20011212	CZ 1994-662	19920922
EP 1193252	A2	20020403	EP 2002-688	19920922
EP 1193252	A3	20031105		
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CN 1075718	A	19930901	CN 1992-112482	19920923
CN 1058714	B	20001122		
AU 9339837	A1	19930819	AU 1993-39837	19930527
AU 642391	B3	19931014		
RU 2098413	C1	19971210	RU 1994-19168	19940321
FI 9401323	A	19940322	FI 1994-1323	19940322
FI 109796	B1	20021015		
NO 9401020	A	19940520	NO 1994-1020	19940322
NO 305120	B1	19990406		
TW 396159	B	20000701	TW 1994-83103422	19940418
US 5539103	A	19960723	US 1994-351532	19941207
US 5723634	A	19980303	US 1995-483309	19950607
US 6066747	A	20000523	US 1995-522307	19951030
US 6069260	A	20000530	US 1997-941640	19970930
GR 3031704	T3	20000229	GR 1999-402796	19991103
US 6479678	B1	20021112	US 2000-517791	20000302
US 2001014746	A1	20010816	US 2001-804821	20010313
US 6562962	B2	20030513		
US 2003027855	A1	20030206	US 2002-208418	20020730
US 6710191	B2	20040323		
US 2003120096	A1	20030626	US 2002-289103	20021106
US 6683196	B2	20040127		
JP 2004043439	A2	20040212	JP 2003-128200	20030506
US 2004073048	A1	20040415	US 2003-673897	20030929
US 7074945	B2	20060711		

PRIORITY APPLN. INFO.:

US 1991-763805	A	19910923
US 1992-862778	A	19920403
US 1992-862955	A	19920403
US 1992-863451	A	19920403
US 1992-863840	A	19920406
US 1992-863849	A	19920406
US 1992-900408	A	19920618
CA 1992-2077394	A3	19920902
CA 1992-2098478	A3	19920922
CS 1994-660	A	19920922

CN Benzenepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -hydroxy-,  
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-  
tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
ester, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM 'C07C229-08  
ICS C07C229-10; C07C229-34; C07D305-14; C07D307-42; C07D307-46;  
C07D307-52; C07D317-50; C07D407-12; C07D409-12  
CC 30-20 (Terpenes and Terpenoids)  
IT 33069-62-4P, Taxol 149197-23-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, from (triethylsilyl)baccatin III and azetidinone  
derivative)

L49 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1993:517582 CAPLUS  
DOCUMENT NUMBER: 119:117582  
TITLE: Metal alkoxides of baccatin III  
INVENTOR(S): Holton, Robert A.  
PATENT ASSIGNEE(S): Florida State University, USA  
SOURCE: PCT Int. Appl., 29 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 28  
PATENT INFORMATION:

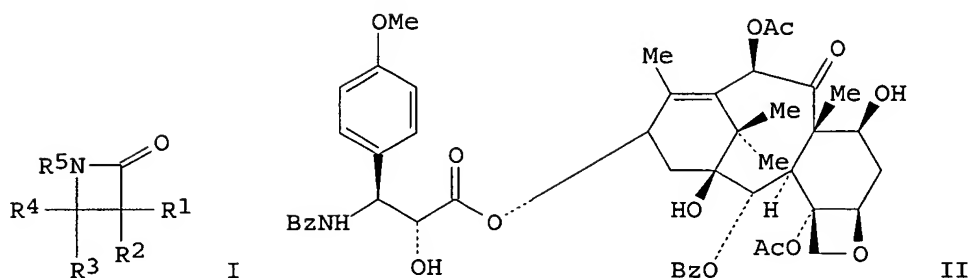
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9306094	A1	19930401	WO 1992-US7952	19920922
W: AU, CA, CS, FI, HU, JP, KP, KR, NO, PL, RU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
US 5229526	A	19930720	US 1992-862778	19920403
CA 2221190	AA	19920902	CA 1992-2221190	19920902
CA 2221190	C	20020212		
ZA 9206827	A	19930315	ZA 1992-6827	19920908
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ZA 9207038	A	19930514	ZA 1992-7038	19920915
ZA 9207039	A	19931220	ZA 1992-7039	19920915
IL 103192	A1	19970610	IL 1992-103192	19920916

US 6683196	B2	20040127		
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PRIORITY APPLN. INFO.:

US 1991-763805	A	19910923
US 1992-862955	A	19920403
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US 1992-863849	A	19920406
US 1992-900408	A	19920618
CA 1992-2077394	A3	19920902
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CS 1994-660	A	19920922
CS 1994-661	A	19920922
EP 1992-921316	A3	19920922
EP 1998-114788	A3	19920922
JP 1993-506299	A3	19920922
US 1992-949107	B3	19920922
WO 1992-US7990	A	19920922
US 1992-967998	B1	19921026
WO 1994-US2382	W	19940304
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US 1996-607108	A1	19960226
US 1997-941640	A1	19970930
US 2000-517791	A1	20000302
US 2000-566970	A1	20000509
US 2002-194343	A1	20020712
US 2002-289103	A1	20021106

OTHER SOURCE(S): MARPAT 119:139574  
GI



AB A metal alkoxide MOCE1E2E3 (M = alkali metal, E1, E2, E3 = H, aliphatic, aryl, alkanoyloxy) is reacted with a  $\beta$ -lactam I [R1 = (un)protected OH, SH, NH<sub>2</sub>, R2 = H, aliphatic, aryl, heteroaryl, R3, R4 = aliphatic, aryl, heteroaryl, acyl, R5 = acyl, carboxy, thiocarboxy, amido, sulfonyl, phosphoryl] to give isoserine esters R<sup>5</sup>NHCR<sup>3</sup>R<sup>4</sup>CR<sup>1</sup>R<sup>2</sup>CO<sub>2</sub>CE1E2E3 which are reacted with a metal derivative of a taxol derivative to give appropriately substituted isoserine esters, e.g. II.

IT 149197-23-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, from (triethylsilyl)baccatin III and azetidinone derivative)

RN 149197-23-9 CAPLUS

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 28  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9306079	A1	19930401	WO 1992-US7990	19920922
W: AU, CA, CS, FI, HU, JP, KP, KR, NO, PL, RU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
CA 2221190	AA	19920902	CA 1992-2221190	19920902
CA 2221190	C	20020212		
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ZA 9206828	A	19930315	ZA 1992-6828	19920908
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ZA 9207038	A	19930514	ZA 1992-7038	19920915
ZA 9207039	A	19931220	ZA 1992-7039	19920915
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CA 2254273	C	20030325		
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CA 2098478	C	19990914		
AU 9226890	A1	19930427	AU 1992-26890	19920922
AU 647971	B2	19940331		
EP 605637	A1	19940713	EP 1992-921316	19920922
EP 605637	B1	19990324		
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JP 07502983	T2	19950330	JP 1993-506299	19920922
JP 3469237	B2	20031125		
HU 71795	A2	19960228	HU 1994-830	19920922
EP 884314	A2	19981216	EP 1998-114788	19920922
EP 884314	A3	20020502		
EP 884314	B1	20040121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE				
RU 2128654	C1	19990410	RU 1994-44324	19920922
AT 178060	E	19990415	AT 1992-921316	19920922
ES 2132129	T3	19990816	ES 1992-921316	19920922
CZ 287417	B6	20001115	CZ 1994-660	19920922
CZ 287609	B6	20010117	CZ 1994-661	19920922
EP 1193252	A2	20020403	EP 2002-688	19920922
EP 1193252	A3	20031105		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE				
AT 258171	E	20040215	AT 1998-114788	19920922
ES 2214665	T3	20040916	ES 1998-114788	19920922
AU 9339838	A1	19930819	AU 1993-39838	19930527
AU 642392	B3	19931014		
FI 9401325	A	19940504	FI 1994-1325	19940322
FI 113046	B1	20040227		
NO 9401022	A	19940520	NO 1994-1022	19940322
NO 306209	B1	19991004		
TW 396159	B	20000701	TW 1994-83103422	19940418
US 5539103	A	19960723	US 1994-351532	19941207
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US 6066747	A	20000523	US 1995-522307	19951030
US 6069260	A	20000530	US 1997-941640	19970930
US 6479678	B1	20021112	US 2000-517791	20000302
US 2001014746	A1	20010816	US 2001-804821	20010313
US 6562962	B2	20030513		
US 2003027855	A1	20030206	US 2002-208418	20020730
US 6710191	B2	20040323		
US 2003120096	A1	20030626	US 2002-289103	20021106

AB Taxane derivs. I [R1 is butenyl, R3 is Ph, T1 is hydrogen, hydroxyl protecting group, or COT2, T2 is H, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl or monocyclic aryl, Ac is acetyl, and E1 and E2 are independently selected from hydrogen and hydroxyl protecting groups] are prepared as antitumor agents. Treatment of 7-triethylsilyl baccatin III with BuLi, followed by reaction with cis-1-benzoyl-3-triethylsilyloxy-4-(2-methyl-1-propenyl)azetidin-2-one and hydrolysis in the presence of HF and pyridine, gave 3'-desphenyl-3'-(2-methyl-1-propenyl) taxol (II). II in vitro showed IC50 of 0.001 (unit unspecified) against human colon carcinoma cells HCT-116, vs. 0.004 for taxol.

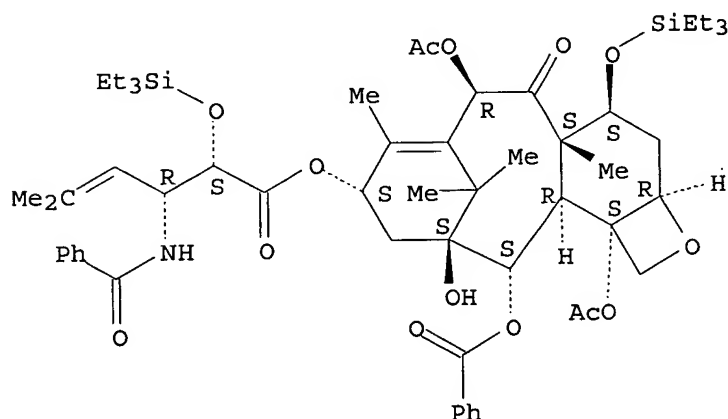
IT 155897-88-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 155897-88-4 CAPLUS

CN 4-Hexenoic acid, 3-benzoyl-5-methyl-2-[(triethylsilyl)oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9a(2S\*,3R\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-335

ICS C07D305-14

INCL 514449000

CC 26-9 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 1

IT 155897-88-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

L49 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:539574 CAPLUS

DOCUMENT NUMBER: 119:139574

TITLE: Preparation of substituted isoserine esters using metal alkoxides and (beta)-lactams

INVENTOR(S): Holton, Robert A.

PATENT ASSIGNEE(S): Florida State University, USA

SOURCE: PCT Int. Appl., 82 pp.

CODEN: PIXXD2



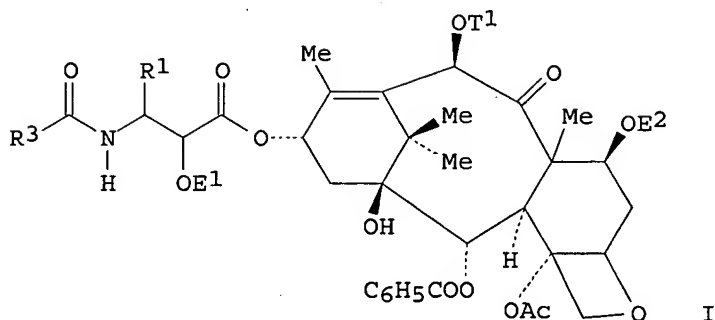
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PRIORITY APPLN. INFO.:

A1 20040415  
B2 20060711

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US 1992-862955 B2 19920403  
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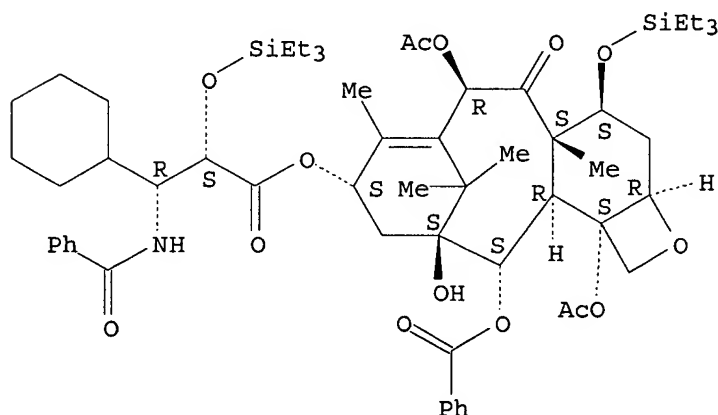
OTHER SOURCE(S): MARPAT 121:35197  
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ES 2206465	T3	20040516	ES 1994-902223	19931101
AT 307577	E	20051115	AT 2002-19283	19931101
ES 2252368	T3	20060516	ES 2002-19283	19931101
ZA 9308217	A	19940719	ZA 1993-8217	19931103
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US 6066747	A	20000523	US 1995-522307	19951030
AU 9726210	A1	19970918	AU 1997-26210	19970623
AU 706985	B2	19990701		
US 6069260	A	20000530	US 1997-941640	19970930
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CN 1270958	A	20001025	CN 1999-118060	19990818
US 6395895	B1	20020528	US 1999-427973	19991027
US 6479678	B1	20021112	US 2000-517791	20000302
US 2001014746	A1	20010816	US 2001-804821	20010313
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US 2003027855	A1	20030206	US 2002-208418	20020730
US 6710191	B2	20040323		
US 2003120096	A1	20030626	US 2002-289103	20021106
US 6683196	B2	20040127		
JP 2004043439	A2	20040212	JP 2003-128200	20030506

CN Cyclohexanepropanoic acid,  $\beta$ -(benzoylamino)- $\alpha$ -  
 [(triethylsilyl)oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-  
 cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-  
 [2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*)],11 $\alpha$   
 ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-335

ICS C07D305-14

INCL 514449000

CC 30-20 (Terpenes and Terpenoids)

Section cross-reference(s): 1

IT 156767-25-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

L49 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:435197 CAPLUS

DOCUMENT NUMBER: 121:35197

TITLE: Preparation of butenyl substituted taxanes as  
 antitumor agents

INVENTOR(S): Holton, Robert A.; Nadizadeh, Hossain

PATENT ASSIGNEE(S): Florida State University, USA

SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 949,107.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

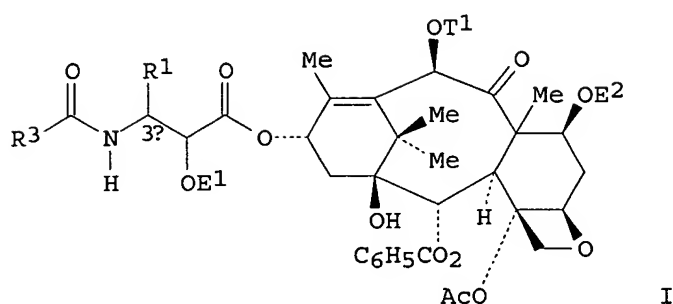
FAMILY ACC. NUM. COUNT: 28

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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CA 2221190	AA	19920902	CA 1992-2221190	19920902
CA 2221190	C	20020212		
ZA 9206827	A	19930315	ZA 1992-6827	19920908
ZA 9206828	A	19930315	ZA 1992-6828	19920908
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CS 1994-660	A 19920922
CS 1994-661	A 19920922
EP 1992-921316	A3 19920922
EP 1998-114788	A3 19920922
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US 1994-351532	A3 19941207
US 1995-462125	A1 19950605
US 1995-483309	A3 19950607
US 1996-607108	A1 19960226
US 1997-941640	A1 19970930
US 2000-517791	A1 20000302
US 2000-566970	A1 20000509
US 2002-134762	A3 20020429
US 2002-194343	A1 20020712
US 2002-289103	A1 20021106

OTHER SOURCE(S): MARPAT 121:109330  
GI



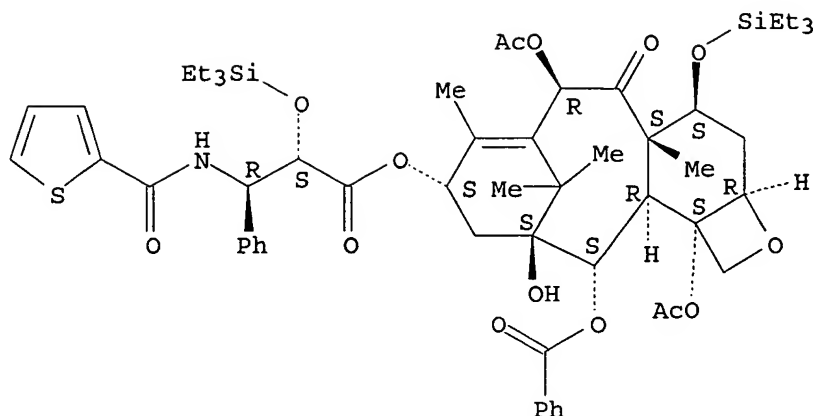
AB Taxane derivs. (I; R1 = cyclohexyl; R3 = Ph; T1 = H, hydroxyl protecting group, or -COT2, T2 = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl or monocyclic aryl; E1, E2 = H, functional groups which increase water solubility), were prepared. Thus, 7-triethylsilylbaccatin III in THF at -45° was treated with BuLi and then cis-1-benzoyl-3-triethylsilyloxy-4-cyclohexylazetidine-2-one; the mixture was warmed to 0° and stirred 1h to give (2'R,3'S)-2',7-bistriethylsilyl-3'-desphenyl-3'-cyclohexyltaxol, which was stirred with aqueous HF and pyridine in acetonitrile to give 73% 3'-desphenyl-3'-cyclohexyltaxol (II). II and taxol showed IC50 = 0.100 and 0.536, resp., against HCT116/VM46.

IT 156767-25-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 156767-25-8 CAPLUS

PRIORITY APPLN. INFO.:

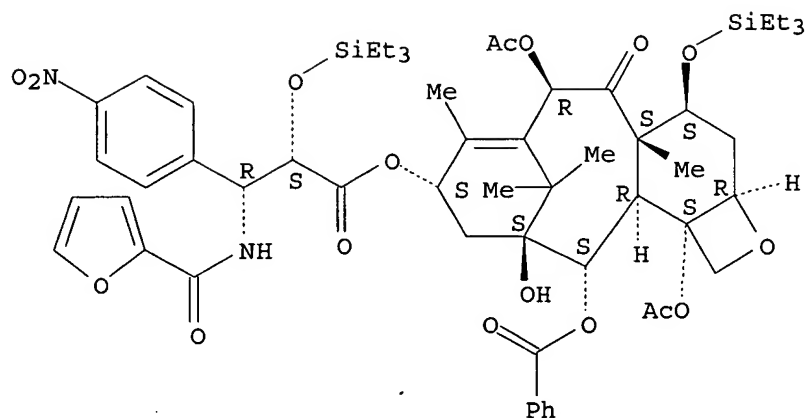
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US 1992-949107	A2 19920922
US 1989-359634	YY 19890531
US 1989-415028	A1 19890929
US 1992-863451	A 19920403
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US 1992-900408	A 19920618
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CA 1992-2098478	A3 19920922



IC ICM A61K031-34  
ICS A61K031-38; C07D305-14  
INCL 514444000  
CC 30-20 (Terpenes and Terpenoids)  
Section cross-reference(s): 1  
IT 157187-81-0P 157187-82-1P 157187-83-2P 157241-41-3P  
157241-42-4P 157241-43-5P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, in preparation of neoplasm inhibitor)

L49 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1994:509330 CAPLUS  
DOCUMENT NUMBER: 121:109330  
TITLE: Preparation of cyclohexyl-substituted taxanes as anticancer drugs.  
INVENTOR(S): Holton, Robert A.; Nadizadeh, Hossain  
PATENT ASSIGNEE(S): Florida State University, USA  
SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 949,107.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 28  
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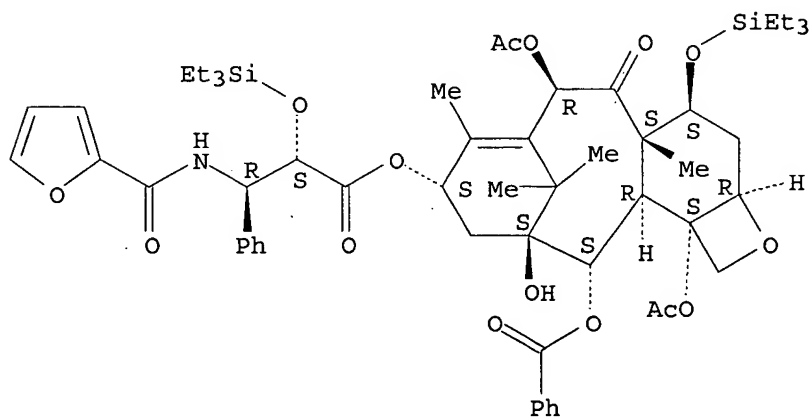
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US 5284865	A	19940208	US 1992-976331	19921113
CA 2221190	AA	19920902	CA 1992-2221190	19920902
CA 2221190	C	20020212		
ZA 9206827	A	19930315	ZA 1992-6827	19920908
ZA 9206828	A	19930315	ZA 1992-6828	19920908
ZA 9206829	A	19930315	ZA 1992-6829	19920908
ZA 9207038	A	19930514	ZA 1992-7038	19920915
ZA 9207039	A	19931220	ZA 1992-7039	19920915
IL 103191	A1	20010724	IL 1992-103191	19920916
CA 2254273	AA	19920922	CA 1992-2254273	19920922
CA 2254273	C	20030325		
EP 884314	A2	19981216	EP 1998-114788	19920922
EP 884314	A3	20020502		
EP 884314	B1	20040121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE				
CZ 287417	B6	20001115	CZ 1994-660	19920922



RN 157241-42-4 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[(2-furanylcarbonyl)amino]- $\alpha$ -[(triethylsilyl)oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 157241-43-5 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[(2-thienylcarbonyl)amino]- $\alpha$ -[(triethylsilyl)oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

JP 1993-506299	A3 19920922
US 1992-967998	B1 19921026
US 1992-968003	A3 19921026
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US 1993-34852	B2 19930322
US 1993-94566	B1 19930720
WO 1993-US10473	W 19931101
WO 1994-US2382	W 19940304
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US 2000-566970	A1 20000509
US 2002-194343	A1 20020712
US 2002-289103	A1 20021106

OTHER SOURCE(S):            MARPAT 121:134497  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. (I; R1 = Ph, p-nitrophenyl; R3 = furyl, thienyl; T1 = H, hydroxyl protecting group, COT2; T2 = H, alkyl, alkenyl, alkynyl, monocyclic aryl; E1, E2 = H, functional groups which increase the water solubility of the taxane derivative), were prepared as antitumor agents. Thus, 7-triethylsilylbaccatin III in THF at -45° was treated with BuLi and then with cis-1-furoyl-3-triethylsilyloxy-4-(4-nitrophenyl)azetidin-2-one followed by stirring to 0° to give a coupling product as a mixture of diastereomers. The crude product was treated with HF in acetonitrile/pyridine to give title compound II. II inhibited HCT 116 and HCT VM46 human colon carcinoma cells with IC50 = 0.002 and 0.883, resp. (no units given).

IT 157241-41-3P 157241-42-4P 157241-43-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, in preparation of neoplasm inhibitor)

RN 157241-41-3 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[(2-furanylcarbonyl)amino]-4-nitro- $\alpha$ -[(triethylsilyl)oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*)],11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE  
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 CZ 287609 B6 20010117 CZ 1994-661 19920922  
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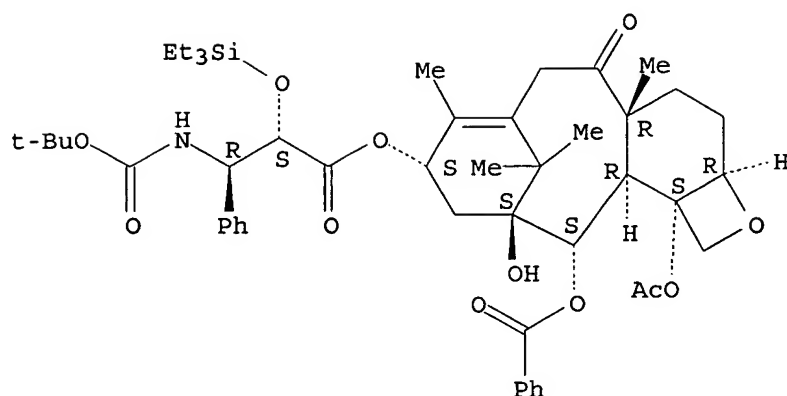
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 CN 1048982 B 20000202  
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 WO 9411362 A1 19940526 WO 1993-US10473 19931101

W: AU, CA, FI, HU, JP, KR, NO, NZ, PL, RU  
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 ES 2130390 T3 19990701 ES 1994-900474 19931101  
 ZA 9308214 A 19940719 ZA 1993-8214 19931103  
 IL 107553 A1 19971120 IL 1993-107553 19931110  
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PRIORITY APPLN. INFO.:

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 CA 1992-2098478 A3 19920922  
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 CS 1994-661 A 19920922  
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 EP 1998-114788 A3 19920922



IC ICM A61K031-355  
ICS C07D305-14  
CC 30-20 (Terpenes and Terpenoids)  
Section cross-reference(s): 1  
IT 159406-32-3P 159406-33-4P 159406-34-5P  
159406-35-6P 159406-36-7P 159406-37-8P  
159406-38-9P 159406-39-0P 159406-40-3P  
159406-41-4P 159406-42-5P  
RL: BYP (Byproduct); PREP (Preparation)  
(byproduct; preparation of C-10 taxane derivs. as antileukemia and antitumor agents)

L49 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:534497 CAPLUS

DOCUMENT NUMBER: 121:134497

TITLE: Preparation of furylcarbonyl- or thienylcarbonyl-substituted taxanes as neoplasm inhibitors.

INVENTOR(S): Holton, Robert A.; Rengan, Kasthuri; Nadizadeh, Hossain

PATENT ASSIGNEE(S): Florida State University, USA

SOURCE: U.S., 13 pp. Cont.-in-part of U.S. Ser. No. 949,107.  
CODEN: USXXAM

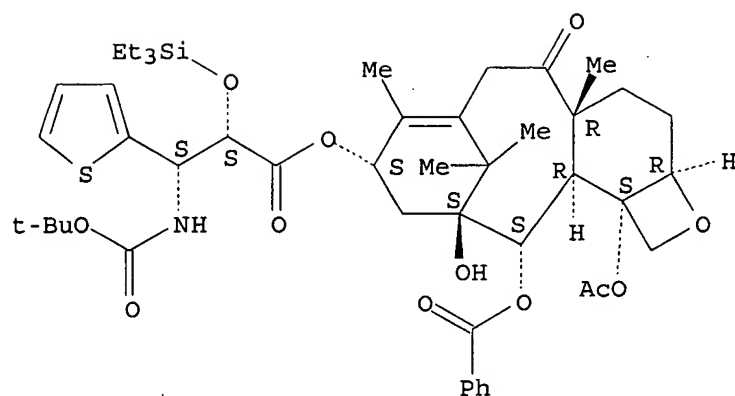
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 28

PATENT INFORMATION:

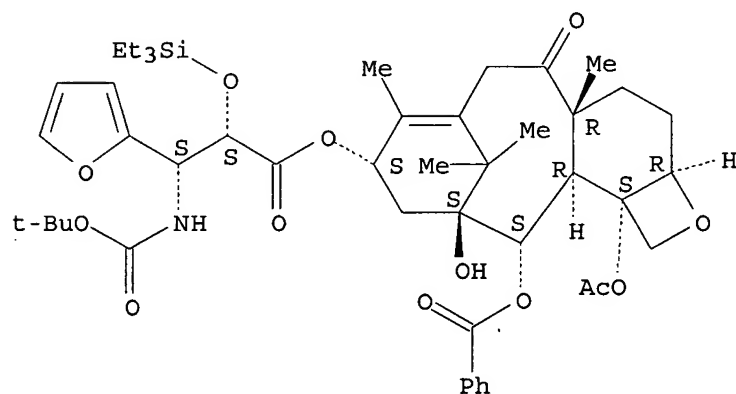
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5283253	A	19940201	US 1992-975723	19921113
CA 2221190	AA	19920902	CA 1992-2221190	19920902
CA 2221190	C	20020212		
ZA 9206827	A	19930315	ZA 1992-6827	19920908
ZA 9206828	A	19930315	ZA 1992-6828	19920908
ZA 9206829	A	19930315	ZA 1992-6829	19920908
ZA 9207038	A	19930514	ZA 1992-7038	19920915
ZA 9207039	A	19931220	ZA 1992-7039	19920915
IL 103191	A1	20010724	IL 1992-103191	19920916
CA 2254273	AA	19920922	CA 1992-2254273	19920922
CA 2254273	C	20030325		
EP 884314	A2	19981216	EP 1998-114788	19920922
EP 884314	A3	20020502		
EP 884314	B1	20040121		



RN 159406-41-4 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy) carbonyl] amino] -  
 $\alpha$ -[(triethylsilyl)oxy]-, 12b-(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
 ester, [2aR-[2a $\alpha$ ,4a $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*),11 $\alpha$ ,12.  
 alpha.,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

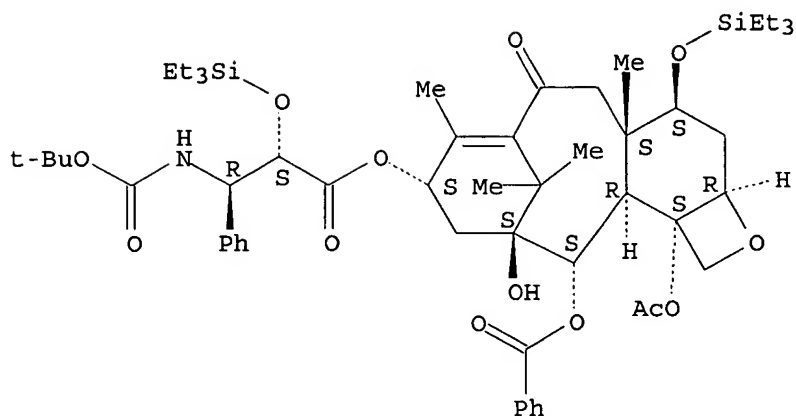
Absolute stereochemistry.



RN 159406-42-5 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy) carbonyl] amino] -  
 $\alpha$ -[(triethylsilyl)oxy]-, 12b-(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl  
 ester, [2aR-[2a $\alpha$ ,4a $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*),11 $\alpha$ ,12.  
 alpha.,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

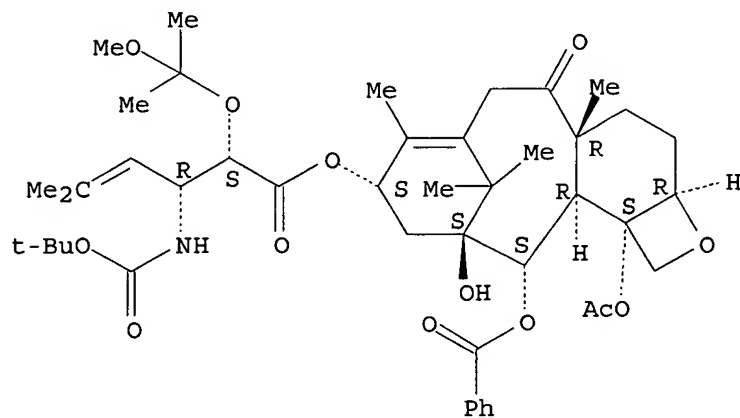
Absolute stereochemistry.



RN 159406-39-0 CAPLUS

CN 4-Hexenoic acid, 3-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-(1-methoxy-1-methylethoxy)-5-methyl-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4aβ,9α(2S\*,3R\*),11α,12α,12a.α,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

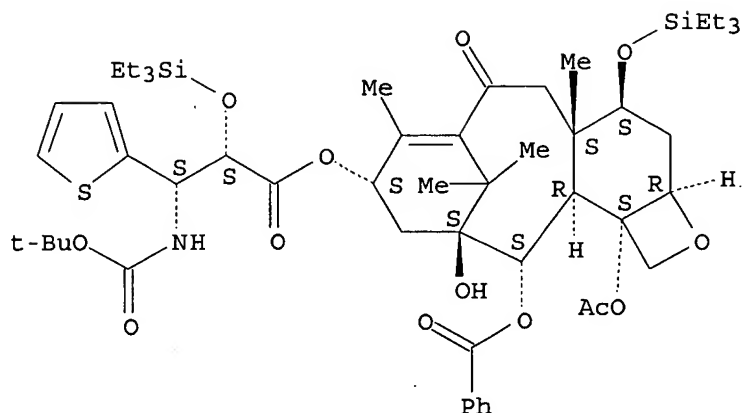


RN 159406-40-3 CAPLUS

CN 2-Thiophenepropanoic acid, β-[[[(1,1-dimethylethoxy)carbonyl]amino]-α-[(triethylsilyl)oxy]-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4aβ,9α(αS\*,βS\*),11α,12.α,12α,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

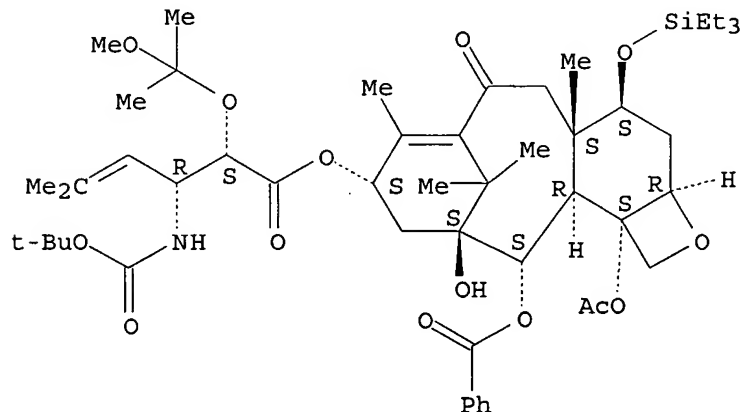
Absolute stereochemistry.



RN 159406-37-8 CAPLUS

CN 4-Hexenoic acid, 3-[[[(1,1-dimethylethoxy) carbonyl] amino]-2-(1-methoxy-1-methylethoxy)-5-methyl-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-6-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4β,4aβ,9α(2S\*,3R\*),11α,12α,12a.α,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



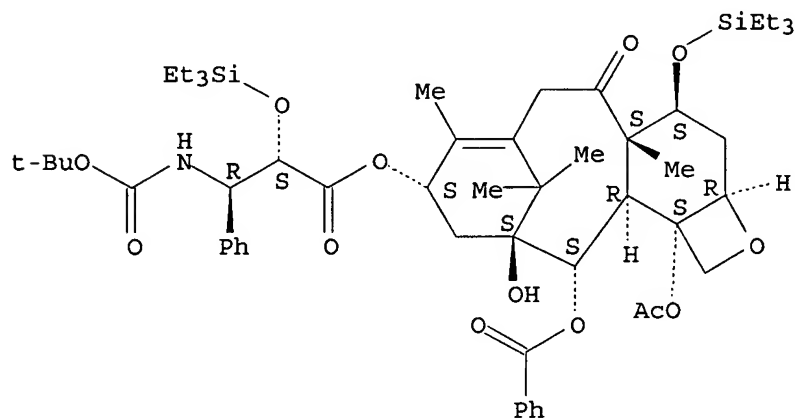
RN 159406-38-9 CAPLUS

CN Benzenepropanoic acid, β-[[[(1,1-dimethylethoxy) carbonyl] amino]-α-[(triethylsilyl)oxy]-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-6-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4β,4aβ,9α(αS\*,βR\*),11α,12.α,12aα,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*)],11 $\alpha$ ,12.alpha.a.,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

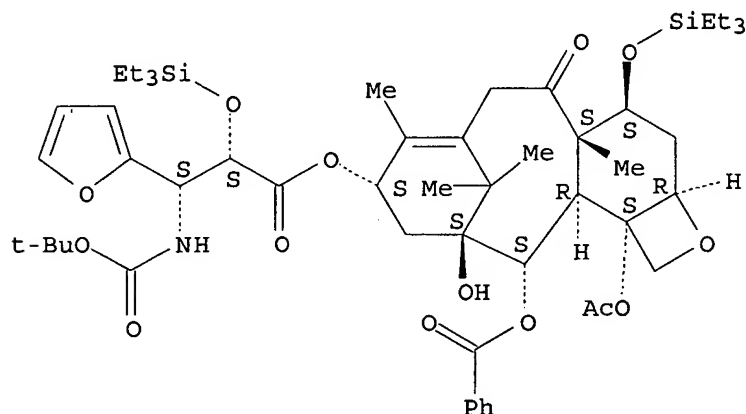
Absolute stereochemistry.



RN 159406-35-6 CAPLUS

CN 2-Furanpropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -[(triethylsilyl)oxy]-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*)],11 $\alpha$ ,12.alpha.a.,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

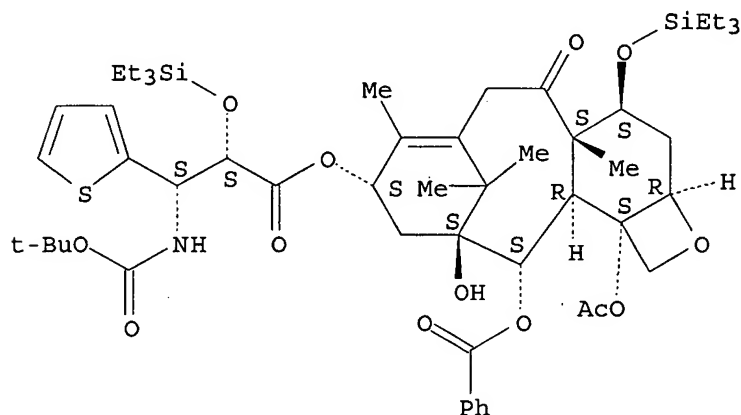


RN 159406-36-7 CAPLUS

CN 2-Thiophenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -[(triethylsilyl)oxy]-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-6-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*)],11 $\alpha$ ,12.alpha.a.,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

CN 2-Thiophenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy) carbonyl] amino] -  
 $\alpha$ -[(triethylsilyl) oxy]-, 12b-(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-4-[(triethylsilyl) oxy]-7,11-methano-1H-  
 cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-  
 [2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ S\*)],11 $\alpha$ ,12.alpha  
 a.,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

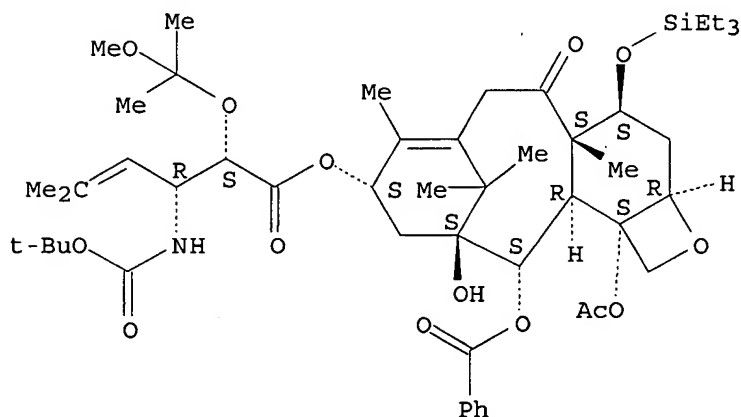
Absolute stereochemistry.



RN 159406-33-4 CAPLUS

CN 4-Hexenoic acid, 3-[[[(1,1-dimethylethoxy) carbonyl] amino]-2-(1-methoxy-1-  
 methylethoxy)-5-methyl-, 12b-(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-4-[(triethylsilyl) oxy]-7,11-methano-1H-  
 cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-  
 [2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,9 $\alpha$ (2S\*,3R\*)],11 $\alpha$ ,12 $\alpha$ ,12a.alpha  
 a.,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

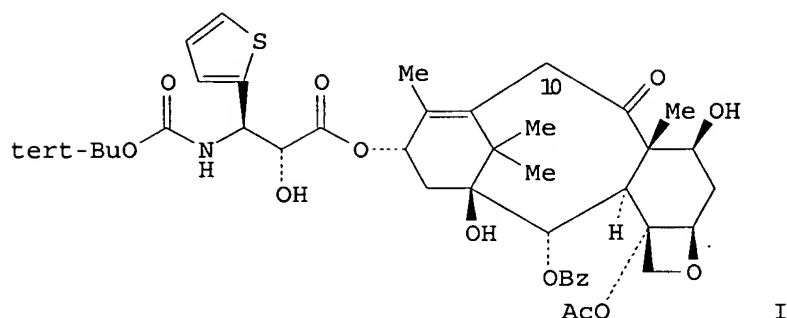


RN 159406-34-5 CAPLUS

CN Benzenepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy) carbonyl] amino] -  
 $\alpha$ -[(triethylsilyl) oxy]-, 12b-(acetyloxy)-12-(benzoyloxy)-  
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-  
 tetramethyl-5-oxo-4-[(triethylsilyl) oxy]-7,11-methano-1H-

US 1993-34852	A 19930322
US 1993-94545	A 19930720
US 1993-10798	A 19930129
US 1993-26978	A 19930305
US 1993-94717	A 19930720
US 1993-95087	A 19930720
US 1993-95160	A 19930720
EP 1994-909453	A3 19940114
WO 1994-US479	W 19940114
EP 1994-909514	A3 19940128
JP 1994-517370	A3 19940128
EP 1994-909840	A3 19940301
WO 1994-US2210	W 19940301
WO 1994-US2382	W 19940304
EP 1994-911675	A3 19940321
EP 1994-910982	A3 19940929
US 2000-566970	A1 20000509

OTHER SOURCE(S) : CASREACT 122:187818; MARPAT 122:187818  
GI



I

AB Taxane derivs. substituted on the C-10 position with novel substituents (specifically H2 or oxo) are disclosed. A highly complex Markush structure is claimed, and 11 example preps. are given. The compds. have utility as antileukemia and antitumor agents. For example, lithiation of 7-O-triethylsilyl-10-desacetoxybaccatin (III) with LiN(SiMe<sub>3</sub>)<sub>2</sub> in THF, followed by esterification with cis-1-tert-butoxycarbonyl-3-triethylsilyloxy-4-(2-thienyl)azetidin-2-one, gave a triethylsilyl-protected, taxol-derived ester as primarily the (2'R,3'S)-isomer, together with a small amount of (2'S,3'R)-isomer. The mixture was deprotected with HF and pyridine in MeCN to give 91% 3'-desphenyl-3'-(2-thienyl)-N-desbenzoyl-(N-tert-butoxycarbonyl)-10-desacetoxytaxol (I). The other taxane derivs. were similarly prepared from protected azetidinones and baccatin (III) derivs. In an in vitro test against human colon carcinoma cells HCT-116, all I were said to have antiproliferative IC<sub>50</sub> < 0.1 (no units), indicating cytotoxic activity.

IT 159406-32-3P 159406-33-4P 159406-34-5P  
159406-35-6P 159406-36-7P 159406-37-8P  
159406-38-9P 159406-39-0P 159406-40-3P  
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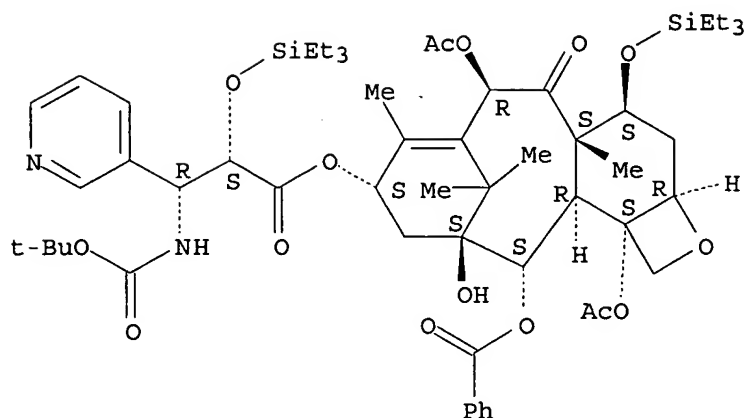
RL: BYP (Byproduct); PREP (Preparation)

(byproduct; preparation of C-10 taxane derivs. as antileukemia and antitumor agents)

RN 159406-32-3 CAPLUS



JP 08505627	T2	19960618	JP 1994-516328	19940114
EP 1211250	A1	20020605	EP 2002-5075	19940114
EP 1211250	B1	20040616		
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AT 225656	E	20021015	AT 1994-909453	19940114
PT 679082	T	20030228	PT 1994-909453	19940114
ES 2184761	T3	20030416	ES 1994-909453	19940114
AT 269315	E	20040715	AT 2002-5075	19940114
PT 1211250	T	20041029	PT 2002-5075	19940114
ES 2225671	T3	20050316	ES 2002-5075	19940114
CN 1495177	A	20040512	CN 2003-2003157907	19940115
EP 1108716	A2	20010620	EP 2001-102159	19940128
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CA 2156908	C	20011002		
WO 9420088	A1	19940915	WO 1994-US2210	19940301
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AU 686137	B2	19980205		
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PT 688212	T	20021129	PT 1994-909840	19940301
ES 2179070	T3	20030116	ES 1994-909840	19940301
IL 108836	A1	20051120	IL 1994-108836	19940303
ZA 9401862	A	19941017	ZA 1994-1862	19940316
ZA 9401899	A	19941018	ZA 1994-1899	19940317
ZA 9401935	A	19941018	ZA 1994-1935	19940318
EP 1227093	A2	20020731	EP 2002-9840	19940321
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EP 1228759	B1	20041215		
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EP 1260223	B1	20050511		
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EP 1398028	A2	20040317	EP 2003-27078	19940321
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US 6066747	A	20000523	US 1995-522307	19951030
US 2003027855	A1	20030206	US 2002-208418	20020730
US 6710191	B2	20040323		
JP 2004043499	A2	20040212	JP 2003-349865	20031008
PRIORITY APPLN. INFO.:			US 1993-5229	A 19930115



IC ICM A61K031-335  
 ICS A61K031-44; C07D405-12; C07D305-14  
 INCL 514337000  
 CC 30-20 (Terpenes and Terpenoids).  
 Section cross-reference(s): 1, 63  
 IT 175840-97-8P 175840-98-9P 175841-00-6P 176017-80-4P  
 176017-81-5P 176017-82-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and pharmaceutical compns. of taxanes having a pyridyl  
 substituted side-chain)

L49 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:219064 CAPLUS

DOCUMENT NUMBER: 122:187818

TITLE: C-10 Taxane derivatives and pharmaceutical  
 compositions containing them as antileukemia and  
 antitumor agents

INVENTOR(S): Holton, Robert A.; Chai, Ki Byung

PATENT ASSIGNEE(S): Florida State University, USA

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

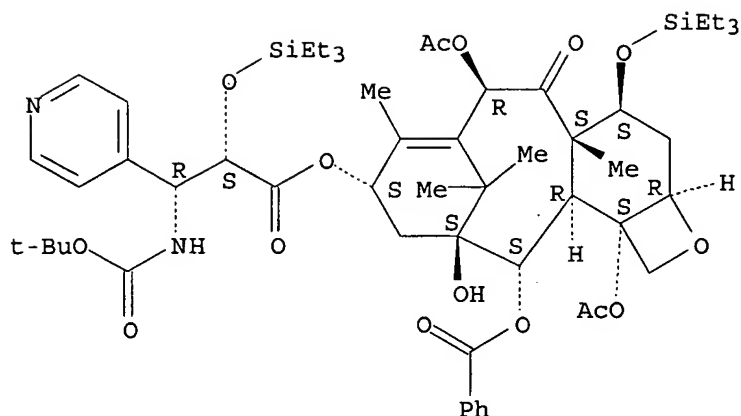
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 28

PATENT INFORMATION:

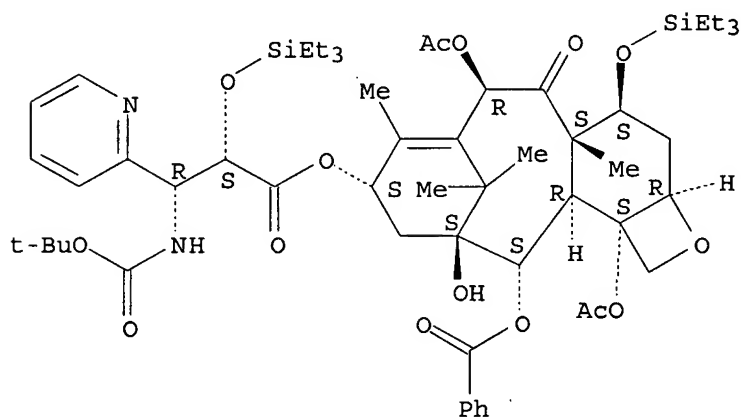
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9415599	A1	19940721	WO 1994-US479	19940114
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US 5338872	A	19940816	US 1993-5229	19930115
CA 2153805	AA	19940721	CA 1994-2153805	19940114
CA 2153805	C	20060328		
CA 2153903	AA	19940721	CA 1994-2153903	19940114
CA 2153903	C	20041102		
AU 9462295	A1	19940815	AU 1994-62295	19940114
AU 682852	B2	19971023		
EP 679082	A1	19951102	EP 1994-909453	19940114
EP 679082	B1	20021009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				



RN 176017-81-5 CAPLUS

CN 2-Pyridinepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -[(triethylsilyl)oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



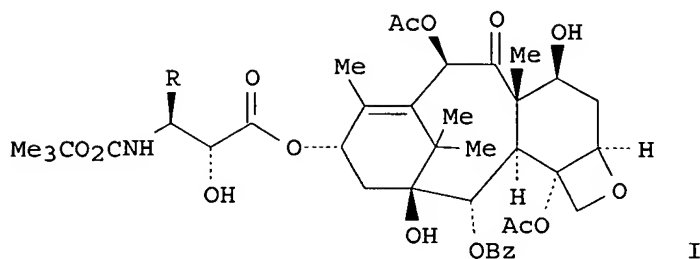
RN 176017-82-6 CAPLUS

CN 3-Pyridinepropanoic acid,  $\beta$ -[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -[(triethylsilyl)oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*),11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

JP 1993-506299	A3 19920922
US 1992-967998	B1 19921026
US 1992-968003	A3 19921026
US 1993-34852	A 19930322
US 1993-95085	A 19930720
WO 1994-US2382	W 19940304
WO 1994-US3094	W 19940321
US 1994-263270	B1 19940621
US 1994-314532	A1 19940928
US 1994-351532	A3 19941207
US 1995-483309	A3 19950607
US 1995-516299	B1 19950817
US 1996-607108	A1 19960226
US 1997-941640	A1 19970930
US 2000-517791	A1 20000302
US 2000-566970	A1 20000509
US 2002-194343	A1 20020712
US 2002-289103	A1 20021106

OTHER SOURCE(S) : MARPAT 124:317534  
GI



AB Taxane derivs. having a 3' pyridyl substituted C13 side chain, e.g. I (R = 2-, 3-, 4-pyridyl) were prepared as anticancer agents. Thus, 7-triethylsilylbaccatin III was treated with cis-1-(tert-butoxycarbonyl)-3-triethylsilyloxy-4-(4-pyridyl)azetidin-2-one followed by desilylation with HF to give I (R = 4-pyridyl). All I had an IC<sub>50</sub> of less than 0.1, indicating they are cytotoxically active.

IT 176017-80-4P 176017-81-5P 176017-82-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and pharmaceutical compns. of taxanes having a pyridyl substituted side-chain)

RN 176017-80-4 CAPLUS

CN 4-Pyridinepropanoic acid,  $\beta$ -[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -[(triethylsilyl)oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2a $\alpha$ ,4 $\beta$ ,4a $\beta$ ,6 $\beta$ ,9 $\alpha$ ( $\alpha$ S\*, $\beta$ R\*)],11 $\alpha$ ,12 $\alpha$ ,12a $\alpha$ ,12b $\alpha$ ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE  
 CZ 287417 B6 20001115 CZ 1994-660 19920922  
 CZ 287609 B6 20010117 CZ 1994-661 19920922  
 EP 1193252 A2 20020403 EP 2002-688 19920922  
 EP 1193252 A3 20031105

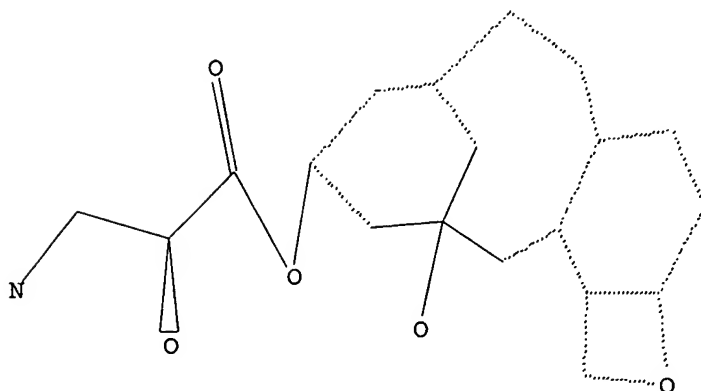
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 SG 97130 A1 20030718 SG 1999-4181 19920922  
 CN 1075315 A 19930818 CN 1992-112286 19920923  
 CN 1048982 B 20000202  
 US 5430160 A 19950704 US 1993-34247 19930322  
 CA 2158863 AA 19940929 CA 1994-2158863 19940321  
 WO 9421252 A1 19940929 WO 1994-US3094 19940321

W: AU, CA, CN, CZ, FI, HU, JP, KR, NO, NZ, PL, RU  
 RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
 AU 9465229 A1 19941011 AU 1994-65229 19940321  
 AU 684768 B2 19980108  
 EP 690712 A1 19960110 EP 1994-912838 19940321  
 EP 690712 B1 20011128

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 JP 08508471 T2 19960910 JP 1994-521329 19940321  
 AT 209489 E 20011215 AT 1994-912838 19940321  
 ES 2164100 T3 20020216 ES 1994-912838 19940321  
 PT 690712 T 20020531 PT 1994-912838 19940321  
 TW 396159 B 20000701 TW 1994-83103422 19940418  
 US 5574156 A 19961112 US 1994-254561 19940606  
 TW 438772 B 20010607 TW 1994-83105964 19940630  
 US 5539103 A 19960723 US 1994-351532 19941207  
 US 5723634 A 19980303 US 1995-483309 19950607  
 US 6066747 A 20000523 US 1995-522307 19951030  
 US 5760219 A 19980602 US 1996-717136 19960920  
 US 6069260 A 20000530 US 1997-941640 19970930  
 AU 9856373 A1 19980430 AU 1998-56373 19980302  
 AU 702492 B2 19990225  
 US 6479678 B1 20021112 US 2000-517791 20000302  
 US 2001014746 A1 20010816 US 2001-804821 20010313  
 US 6562962 B2 20030513  
 US 2003027855 A1 20030206 US 2002-208418 20020730  
 US 6710191 B2 20040323  
 US 2003120096 A1 20030626 US 2002-289103 20021106  
 US 6683196 B2 20040127  
 JP 2004043439 A2 20040212 JP 2003-128200 20030506  
 US 2004073048 A1 20040415 US 2003-673897 20030929  
 US 7074945 B2 20060711

PRIORITY APPLN. INFO.:

US 1991-763805 B2 19910923  
 US 1992-862955 B2 19920403  
 US 1992-863849 B2 19920406  
 US 1992-949107 B2 19920922  
 US 1993-34247 A2 19930322  
 US 1989-359634 YY 19890531  
 US 1989-415028 A1 19890929  
 US 1992-862778 A2 19920403  
 US 1992-863451 A 19920403  
 US 1992-863840 A 19920406  
 US 1992-900408 A 19920618  
 CA 1992-2077394 A3 19920902  
 CA 1992-2098478 A3 19920922  
 CS 1994-660 A 19920922  
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 EP 1998-114788 A3 19920922



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L47      99 SEA FILE=CAPLUS ABB=ON  PLU=ON  HOLTON ROBER?/AU
L49      7 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L45 OR L24) AND (L46 OR L47)
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L49 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:169149 CAPLUS

DOCUMENT NUMBER: 124:317534

TITLE: Preparation and pharmaceutical compositions of taxanes having a pyridyl substituted side-chain

INVENTOR(S): Holton, Robert A.; Rengan, Kasthuri

PATENT ASSIGNEE(S): Florida State University, USA

SOURCE: U.S., 19 pp. Cont.-in-part of U.S. 5,430,160.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 28

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5489601	A	19960206	US 1993-95085	19930720
CA 2221190	AA	19920902	CA 1992-2221190	19920902
CA 2221190	C	20020212		
ZA 9206827	A	19930315	ZA 1992-6827	19920908
ZA 9206828	A	19930315	ZA 1992-6828	19920908
ZA 9206829	A	19930315	ZA 1992-6829	19920908
ZA 9207038	A	19930514	ZA 1992-7038	19920915
ZA 9207039	A	19931220	ZA 1992-7039	19920915
IL 103191	A1	20010724	IL 1992-103191	19920916
CA 2254273	AA	19920922	CA 1992-2254273	19920922
CA 2254273	C	20030325		
EP 884314	A2	19981216	EP 1998-114788	19920922
EP 884314	A3	20020502		
EP 884314	B1	20040121		

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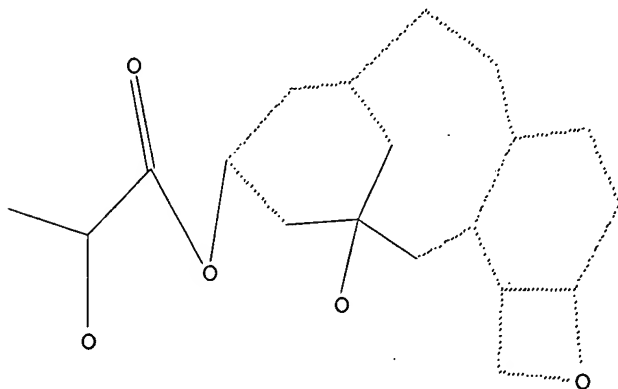
FILE COVERS 1907 - 19 Sep 2006 VOL 145 ISS 13  
FILE LAST UPDATED: 18 Sep 2006 (20060918/ED)

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=> d stat que L49

L3 STR



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L20 STR

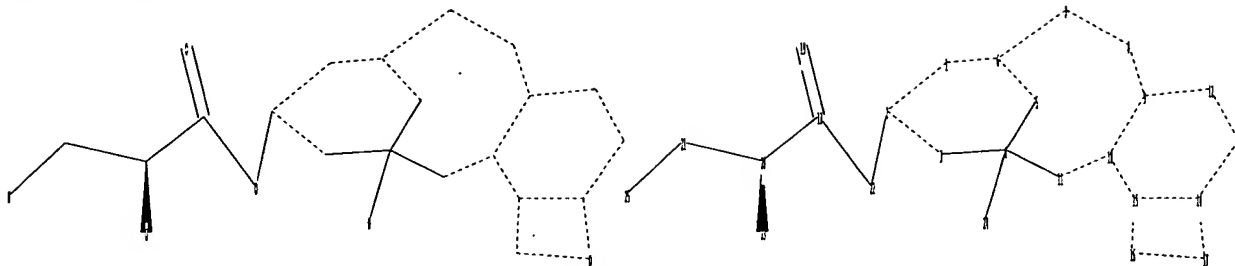
4 (Parity=Even)

Stereo RSS Sets:

Type=Absolute (Default). 1 Nodes= 4

Structure L20:

Uploading L20.str



chain nodes :

18 19 20 22 23 24 25

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17

ring/chain nodes :

21

chain bonds :

2-22 4-24 18-20 18-19 18-22 20-21 20-23 21-25

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-11 5-6 6-7 7-8 8-9 9-10 9-12 10-11 10-15 12-13  
13-14 14-15 14-17 15-16 16-17

exact/norm bonds :

1-2 1-6 2-3 2-22 3-4 4-5 4-11 4-24 5-6 6-7 7-8 8-9 9-10 9-12 10-11  
10-15 12-13 13-14 14-15 14-17 15-16 16-17 18-19 18-22 20-23 21-25

exact bonds :

18-20 20-21

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS  
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS

Stereo Bonds:

23-20 (Single Wedge).

Stereo Chiral Centers:

20 (Parity=Odd)

Stereo RSS Sets:

Type=Absolute (Default). 1 Nodes= 20



exact/norm bonds :

1-2 1-6 2-3 2-22 3-4 4-5 4-11 4-24 5-6 6-7 7-8 8-9 9-10 9-12 10-11  
10-15 12-13 13-14 14-15 14-17 15-16 16-17 18-19 18-22 20-23

exact bonds :

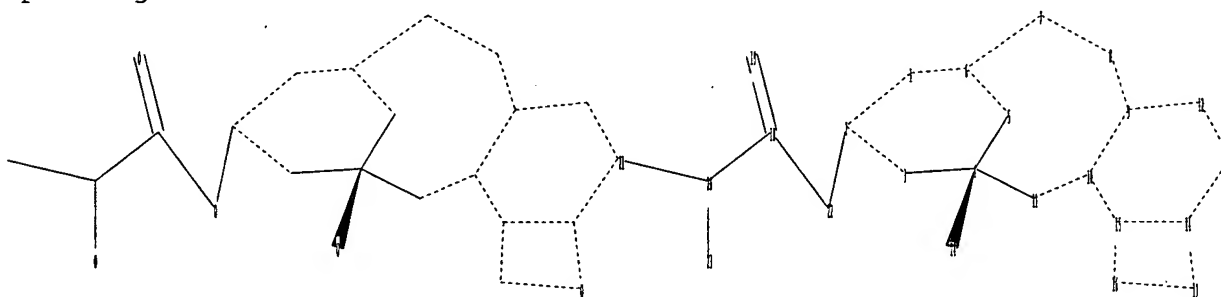
18-20 20-21

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS  
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS

Structure L14:

Uploading L14.str



chain nodes :

18 19 20 22 23 24

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17

ring/chain nodes :

21

chain bonds :

2-22 4-24 18-20 18-19 18-22 20-21 20-23

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-11 5-6 6-7 7-8 8-9 9-10 9-12 10-11 10-15 12-13  
13-14 14-15 14-17 15-16 16-17

exact/norm bonds :

1-2 1-6 2-3 2-22 3-4 4-5 4-11 4-24 5-6 6-7 7-8 8-9 9-10 9-12 10-11  
10-15 12-13 13-14 14-15 14-17 15-16 16-17 18-19 18-22 20-23

exact bonds :

18-20 20-21

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS  
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS

Stereo Bonds:

24-4 (Single Hash).

Stereo Chiral Centers:

=> file registry

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STRUCTURE FILE UPDATES: 18 SEP 2006 HIGHEST RN 907539-37-1

DICTIONARY FILE UPDATES: 18 SEP 2006 HIGHEST RN 907539-37-1

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

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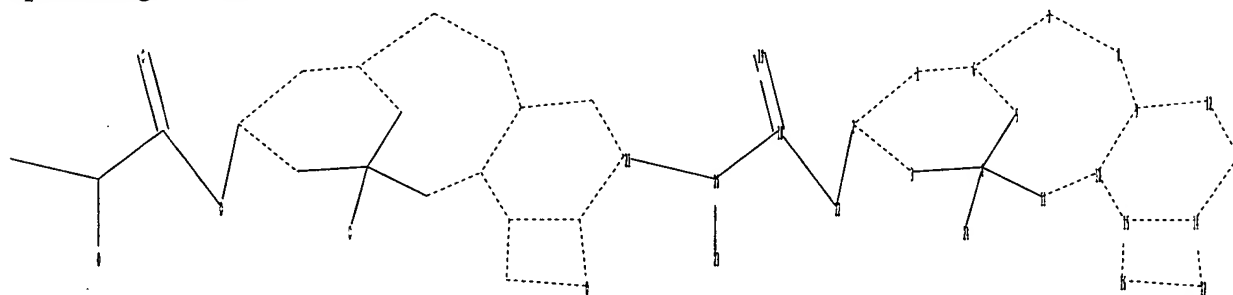
<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Structures searched:

Structure L3:

Uploading L3.str



chain nodes :

18 19 20 22 23 24

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17

ring/chain nodes :

21

chain bonds :

2-22 4-24 18-20 18-19 18-22 20-21 20-23

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-11 5-6 6-7 7-8 8-9 9-10 9-12 10-11 10-15 12-13  
13-14 14-15 14-17 15-16 16-17